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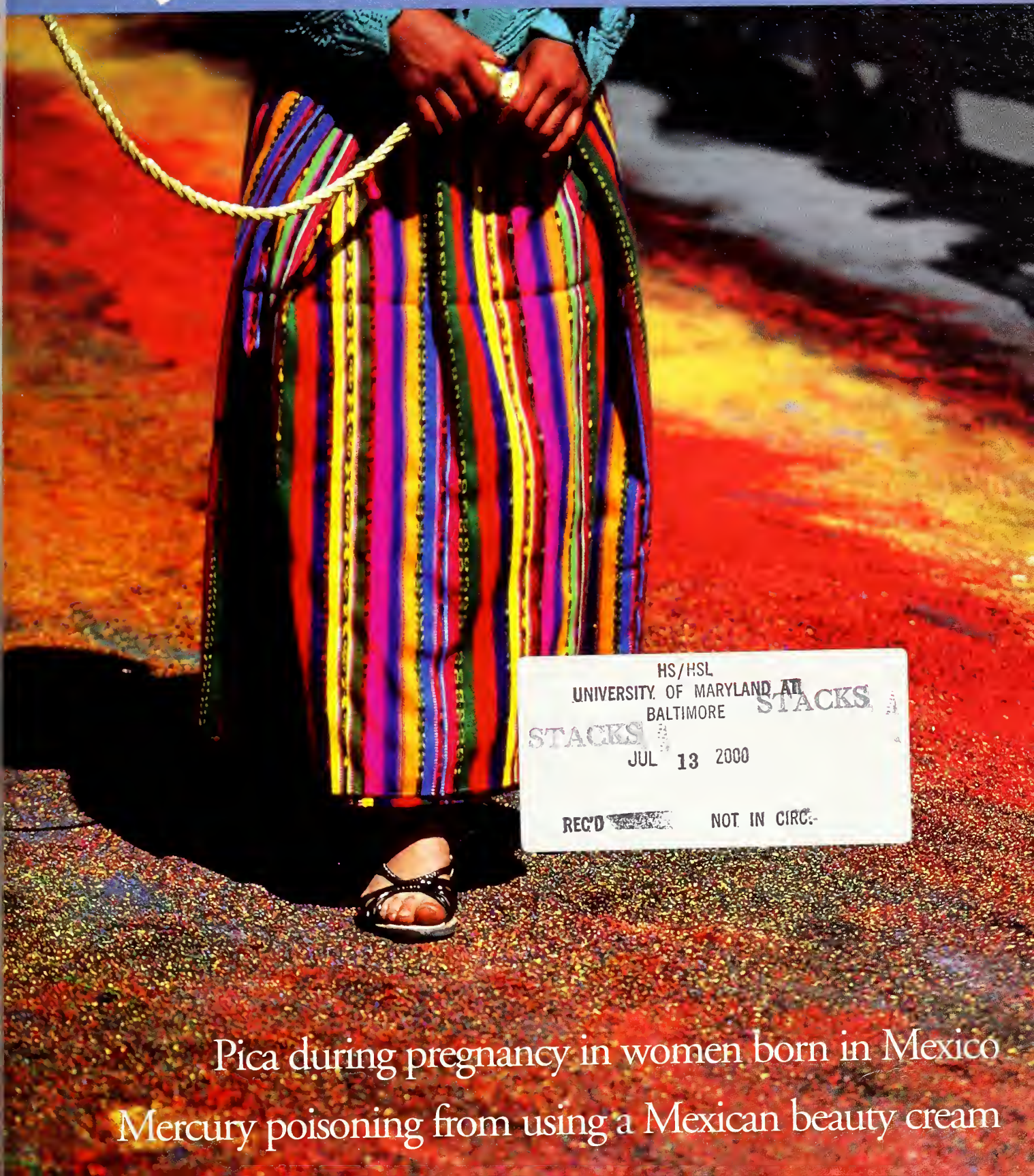

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This month in wjm

Mexican beauty creams can cause mercury poisoning

In September 1995, a 15-year-old adolescent living in Texas near the Mexican border developed a paraparesis. He had been using a Mexican acne cream called "Crema de Belleza," which was found to be rich in mercury. Public announcements about the hazards of the cream were issued in California, Arizona, New Mexico, and Texas. On p 15, Weldon and colleagues report that 330 cream users (96% were women, 95% were Hispanic) contacted their local health department. Testing showed their mean urine mercury concentration was elevated, and there was a high prevalence of symptoms suggestive of poisoning. On p 19, Davis discusses the clinical features of mercury intoxication.

Sunscreen may increase melanoma risk

A growing body of evidence is challenging the assumption that high factor sunscreen offers strong protection against skin cancer. Numeric labeling of sunscreen may be inappropriate, because quantities routinely applied to the skin are only one quarter of those used to measure the protection factor. On p 58, Autier argues that using high factor sunscreen may actually increase cancer risk, because it leads to longer periods of recreational sun exposure. We should focus our advice, he says, on more general protection measures.

Pica is common in pregnant Mexican-born women

Pica, the ingestion of nonfood items, is well described in children. Little is known, however, about its prevalence and causation during pregnancy. Simpson and colleagues (p 20) interviewed pregnant or recently pregnant women in low-income southern Californian communities and in Ensenada, Mexico. The prevalence of pica during pregnancy was 31% in the southern California group and 44% in the Ensenada group. Ingested items included magnesium carbonate, dirt, and clay. In a commentary on p 25, Morales and Hayes-Bautista argue that pica could harm the fetus and the mother.

Sports physicians face conflicts of interest

Sports medicine is thought of as glamorous and lucrative. But sports physicians face their own set of pressures and dilemmas. One of these is the pressure exerted by club managers to allow injured players to return to the game. In an interview by Staunton on p 10, Warren J Strudwick, who treats the Oakland Raiders and the Golden State Warriors, says: "The most important issue is healing the player's injury. That's number one. Compared with that, all other issues are peripheral."

Editor's Pick

My 94-year-old grandmother has metastatic breast cancer, although she does not know the diagnosis. She knows that she is ill, and doesn't want to live forever. She is still mentally alert, holds strong opinions about almost everything, and wants to make her own choices. But what should she be told?

Does detailed information about diagnosis and prognosis empower people or push them into a state of hopelessness, despair, and premature death? Doctors used to adopt a paternalistic approach, sheltering their patients from the details surrounding their illness. They would concoct stories to disguise the truth, making unilateral decisions about was "best" for them.

Slowly, things have changed. Standard practice now requires that mentally competent people be involved in decision-making, thus necessitating discussions of diagnosis. Many patients want to know exactly what is happening to them. Ironically, doctors practicing in our new "health care environment" don't know their patients for a long enough time to provide tailored information. There are many reasons why we don't know our patients the way we used to, including the regularly changing menu of health plans and an increasingly mobile society. But does it matter?

In this month's *wjm*, Leydon and colleagues (p 26) offer some insight based on interviews with 17 newly diagnosed cancer patients. While all patients wanted to know their diagnosis and treatment options, this is all that they had in common. Some wanted specific details with statistics, while others wanted only a summary or very little information at all. The authors found that people's attitudes toward 3 areas—faith in the medical profession, hope, and concern for others—predicted their desires for specific information.

What will my grandmother do with the information that she has cancer? She may ignore it. On the other hand, she may decide to fight the cancer, but I doubt it. It is far more likely that she will accept it, without surprise. Some studies suggest that this type of acceptance may lead to an earlier death compared with denial or a "fighting" approach. But the choice is hers. It is then our duty both as physicians and fellow humans to support her decision and provide compassion, care, and support.

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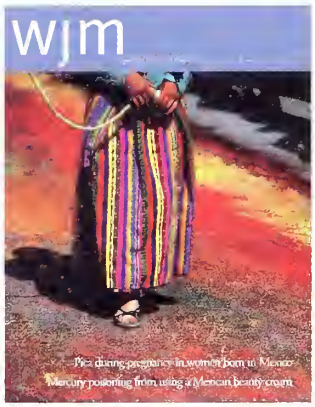

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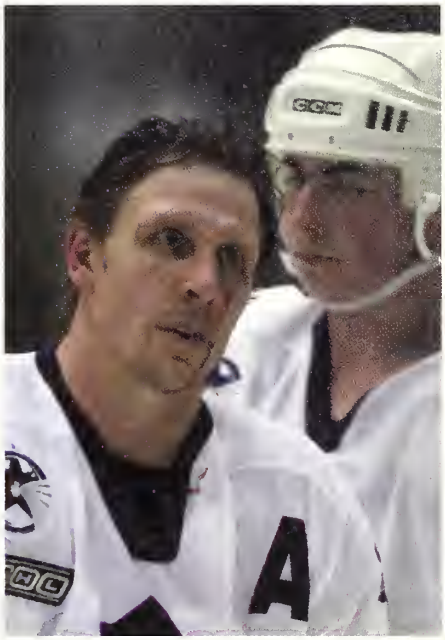

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Op-Ed

Can complementary medicine be evidence-based?

Yes, if it embraces standardization and conventional research tools

Gavin Yamey
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Two years ago, the editors of the *New England Journal of Medicine* declared: "It is time for the scientific community to stop giving alternative medicine a free ride."[1] Here were the voices of orthodoxy, loud and clear, sounding the death knell of complementary and alternative medicine (CAM). Echoing a long history of medical tribalism,[2] CAM was once again under attack for being antiscientific and grounded in unproven narrative.

Since that declaration, CAM practitioners and researchers have tried to defend their practices. They have begun to publish in peer-reviewed biomedical journals, and they recently held an international congress addressing research methodology and quality management.[3] A Cochrane Collaboration will publish a series of papers critically appraising systematic reviews of 30 CAM therapies.[4] All this, despite minimal research funding or infrastructure.

So, is the argument now over? Not quite, for there are still two fundamental conflicts between the "art" of CAM and the "science" of evidence-based medicine. Resolving these conflicts is the key to distinguishing evidence-based complementary medicine from practices based on anecdote.

The first conflict is between standardization and individualization. Evidence-based medicine emphasizes reproducibility. It attempts to define a universal "best practice," based on large randomized controlled trials and meta-analyses. This is the antithesis of CAM, which focuses on the individual interaction between patient and practitioner. Within the personal framework of CAM, no two interactions can ever be the same. Its practitioners argue that the consultation, a complex interplay between two people, is itself therapeutic, and it necessarily defies empiric understanding. Using a randomized controlled trial to measure CAM would be analogous, with this argument, to measuring a delicate rose with a ruler.

But this stance is no longer acceptable. A physician faced with a patient who has a particular disease manifestation needs to know precisely which orthodox or complementary treatment will help. The problem with CAM to date has been that the myriad therapies and their uses have not been adequately defined. David Eisenberg of the Center for Alternative Medicine Research at Harvard University told the congress that there are "so many labels, so little consensus." The first step to making CAM more evidence based must be to codify these treatments and to define their exact therapeutic indications.

Once complementary therapies have been defined in this way, their clinical efficacy can be assessed with the conventional research tools of evidence-based medicine. So, for example, in a randomized controlled trial, the herbal remedy St John's wort was as effective as imipramine for treating moderate depression.[5] In another trial, spinal manipulation was no better than control in treating episodic tension-type headaches.[6]

The second conflict is between faith in the randomized controlled trial as a gold standard for measurement and dissent from this belief. David Reilly, from the Glasgow Homoeopathic Hospital, voiced this tension at the congress, asking: "If you look at the complexity of caring for someone, are the tools adequate to address whether it works?" This question is a challenge to orthodox practitioners, for it asks us whether we are missing something important in CAM when we use standard assessment tools. Are these tools appropriate?

Randomized controlled trials are valued in medicine because they can test for causality, determine effect size, assess risks and benefits of treatments, and minimize selection and measurement bias. It is true that many CAM interventions are difficult to blind or have no satisfactory placebos, but these methodologic problems can be overcome. An example is the development of a "placebo needle" for use in acupuncture research—the placebo looks exactly like an acupuncture needle, and it causes the same dull pain sensation.[7] It does not, however, penetrate the skin, so it allows researchers to examine the specific physiologic effects of acupuncture.

A major criticism of randomized trials is that they fail to address individual patients' experiences of therapy. But evidence-based medicine has a wide range of qualitative tools that can be used to explore these more personal aspects. Qualitative research is an ideal way to examine why and when patients use complementary therapies and to help us understand the enormous benefits they experience. For example, a recent qualitative study addressed the question of why people self-medicate with St John's wort. Users reported previous use of other herbal remedies, a belief in their safety, and a desire to take control of their lives.[8]

Where evidence-based medicine has let doctors and patients down is in ignoring the nonspecific "complex effects" that are a crucial part of the healing process.[9] Indeed, Ted Kaptchuk, also from Harvard's Center for Alternative Medicine Research, believes that the biggest role for CAM could be to bring these effects into the forefront of medicine.[10] Randomized controlled trials at-

tempt to cancel out factors such as the therapeutic setting, the personality of the therapist, the amount of time given to patients, and even the very words spoken to them. Instead of being hidden within the placebo arm, these should be disentangled and studied systematically, so that their therapeutic benefits can be harnessed by all involved in the provision of health care.[11] The art of both orthodox and complementary medicine, Reilly's "complexity of caring," is difficult but not impossible to quantify.[12]

Over 40% of people in the United States use CAM.[13] This huge demand suggests that it offers something of value that is not provided by orthodox medicine. Politicians and policy makers have realized this fact, and a new presidential commission on CAM has been appointed. The tools of evidence-based medicine can help us to understand and explain the popularity of this branch of health care. In a state-funded health system, they can also guide us in spending decisions, ensuring that taxpayers' money is spent on the most effective orthodox and complementary treatments. Evidence-based medicine is a democratizing force, not a divisive one. Researchers and practitioners in the field of complementary medicine have nothing to lose, and much to gain, from embracing it. They should remember the words of an ancient Chinese proverb, quoted by Eisenberg at the congress: "Real gold does not fear even the hottest fire."

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Exercise counseling in health promotion

Primary care providers have a key role

Despite the clear health benefits that can be attained through adopting a more active lifestyle, most adults in industrial nations remain underactive. Faced with this epidemic, there is a growing need for physical activity interventions that can be widely disseminated to all segments of the population across the life span.

One promising avenue of physical activity counseling and support lies with primary care physicians and other health care professionals. The strengths of incorporating physical activity advice and support as part of routine health care include the ability to reach a substantial portion of the population repeatedly over time, the consistency and continuity of message content and delivery, and the willingness of patients to act on their physicians' advice.[1,2] Despite these strengths, however, many barriers to physical activity counseling in primary care have been documented, including lack of time, reimbursement, and training in counseling physical activity or behavior change.[3] Although such barriers present continuing challenges to the health promotion and health care fields, the possible public health effects that primary care settings can have on health behavior change, including physical activity, merit continued investigation.

Although a relatively large body of research exists on advice and counseling by physicians for other health behaviors, such as stopping smoking, relatively little systematic research has been conducted to date on the promotion of physical activity in primary care practices. The studies that have been undertaken have had the advantage of a growing body of knowledge that underscores the utility of applying empirically supported behavioral strategies in aiding physical activity change. Such behavioral strategies, derived primarily from social cognitive theory, include identifying specific practical goals tailored to individual patients' physical activity needs and circumstances; structuring initial patient expectations so that they are realistic; identifying those benefits related to becoming more physically active that are most germane to a patient's health

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status; encouraging patients to keep track of their physical activity patterns through simple self-monitoring tools; and providing continual interest, encouragement, and support for physical activity. Some of these behavioral strategies have been used in studies in which primary care physicians have been trained to give brief advice and counseling on physical activity, with encouraging results in the short term.[4,5] In 1 study, for example, a written goal-oriented exercise prescription from general practitioners, in addition to verbal advice, was particularly effective in promoting increased physical activity during a 6-week period.[6]

More discrepant results obtained from longer term programs involving multiple risk factors, however, suggest that more intensive interventions may be needed to obtain longer term effects in at least some segments of the population. Such interventions could include the use of health educators and professionals in addition to physicians. Health educators and other allied health professionals can provide a level of advice and counseling beyond that which physicians, constrained by time and similar barriers, are typically able to provide.[7] One promising approach awaiting more investigation involves using brief advice from the physician as a means of setting the stage for physical activity change in conjunction with specific referral to other health care–based or community-based health educators or providers. In this way, the perceived credibility and authority of the physician can be harnessed as a catalyst for change, while the real time constraints facing many physicians are recognized.[8] The challenge remains to structure the referral network effectively so that patients will successfully follow through with the referral. To maximize the potential benefits of this type of referral network, continuing communication between the physician and the referral source is essential.

In addition, the studies targeting primary care physicians have focused almost exclusively on those involved in family practice and internal medicine. Yet, other primary care specialists, such as pediatricians and obstetrician-gynecologists, reach important segments of the population for whom physical activity information and messages are particularly relevant. Future research should target the full range of primary care practice.

Although face-to-face instruction and counseling for physical activity have traditionally been the norm in most countries, a growing scientific literature has underscored the usefulness of mediated channels for providing physical activity advice and information in an efficient, effective, and possibly less costly manner. For instance, in the United States, at least 13 randomized controlled investigations have systematically evaluated the use of telephone-based physical activity advice and support, either in conjunction with or independent of advice from the physician.[7,9,10] The telephone-supervised approach has been effective in both older and younger adult populations, women as well as men, patients with heart disease, older family carers of relatives with dementia, and overweight patients. It has been effective in promoting physical activity of various types (endurance, strength, flexibility, and general conditioning), intensities (moderately intense or more vigorous exercise), and formats (home-based, group-based, or combinations of home- and group-based exercise). Telephone and similar mediated approaches allow both the health professional and the patient a level of convenience and flexibility that is often diminished or lacking in group-based physical activity regimens.

To reach the public health goals on physical activity in the United Kingdom, United States, Australia, and other countries, continued efforts to involve primary care physicians and other health professionals as active facilitators of the physical activity message are strongly indicated. Primary care advice in conjunction with referral to appropriate community organizations may help to facilitate the long-term increases in physical activity participation that are critical for health promotion and disease prevention. Telephone and other mediated approaches to physical activity promotion provide a promising avenue for program delivery, in primary care and other community settings.

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Is equity a scientific issue?

Inequality across socioeconomic and political groups influences health outcomes

Equity is a humanitarian issue that derives from principles of ethics, especially justice (fairness). Fairness requires the elimination of inequity—that is, systematic inequality across population subgroups. Can science be brought to bear on the subject of equity? The answer must be yes.

It is no secret that, in the world over and within countries, the rich are getting richer and the poor are getting poorer. Ethical issues alone suggest a cause for alarm on humanitarian grounds. Concern is heightened by the relatively recent evidence that increasing poverty is not the only worry. Although it is a big one, it is not a new one. The new issue concerns the evidence of increasing inequities in wealth wherein the ill effects derive not only from increases in poverty but also because the wealthy are becoming wealthier.

Recent literature is converging on the conclusion that the extent of disparities between the wealthiest segments of society and the least wealthy is directly related to the health of that society, even when health is measured by conventional mortality and morbidity statistics. Thus, the phenomenon is not a matter only of material deprivation among the poorer segments of society,[1-3] and it is not alleviated substantially by providing alms (either public or private) to lighten the burden on the poor.

There are many determinants of ill health, whether at an individual or a population level. Political, socioeconomic, and demographic factors play a crucial role in influencing health outcomes. These operate to increase or decrease risks to illness through genetics, biologic factors, and other pathophysiologic mechanisms. Time and trajectories over the life course also play a part. The influence on adult health of events in early life and continuing through childhood are now undeniable, although the mechanisms of the trajectories are still unclear. Does early damage always increase the risk of subsequent disease, and under what conditions might it not? Might the effects of early insults be occult, only to be manifested later? Are they mostly gradually accumulating, with each increment leading to progressively greater risks to health later on? Or are there vulnerable "incubation" periods during which people are particularly susceptible to incurring risks that will be manifested later on?

We are also beginning to suspect that the pathway of determinants does not act in the same way in all countries, all cultures, and in all population subgroups. For example, in the United States, mortality in black populations in urban areas seems much more heavily influenced by income inequality than is the case in white urban populations, in which the adverse effect of income inequalities is partly mitigated, for example, by greater availability of primary care health services (unpublished data).

The findings regarding the likely importance of primary care in reducing the effect of income inequality, at least in some areas and populations in the United States,[4] run counter to the widely held belief that health services do not have much effect on health. Only a few studies provide any hope for the potential benefits of health services taken together.[5,6] However, newer conceptualizations of health services have brought the realization that they are composed of 2 distinct parts: primary care and specialty care, and at least in terms of population health, it is primary care and not specialty care that contributes the most.[7]

The subject of the causation of inequities in health is clearly complex, but it is amenable to scientific study. The many issues concerning the nature of the pathways in different population groups, in different cohorts, and in different historical time periods are only some of the many challenges. We need good scientific research on the nature of the pathways and their consistency and variability; on the best ways to specify the variables that represent the various types of characteristics in the theoretical models; on the relative influence and mechanisms of effect of various types of interventions to reduce the effects on ill health and, perhaps, even improve the health of populations; and on the special challenges posed by vulnerable population groups, such as children and adolescents, women and especially pregnant women, and racial and ethnic minorities. The development and application of statistical techniques that elucidate mechanisms rather than describe them are also a high priority, as are collaborative efforts across political jurisdictions and countries to improve the generalizability of research results and policy applications.

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News and Features

Guru promotes global health

Abi Berger, London

When David McQueen returned to the United States after 10 years in Scotland, he gained almost 15 pounds. "I started eating just a bit more than I needed to, and I found I needed a car to get around," he said. He wasn't alone in this behavior: overeating and lack of daily exercise are creating major public health problems in the United States.

In Edinburgh, a carless McQueen (a medical sociologist who had trained at Johns Hopkins University School of Public Health) had been the director of a stand-alone research unit in health and behavioral change. From there, in 1992, he was recruited to join the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia.

He is now Associate Director for Global Health Promotion at the agency, a program that includes a wide variety of tasks, from advising countries on vaccination schemes to helping countries tackle problems such as cancer and cardiovascular disease. These last problems have become more critical in recent years as people have started living longer and fewer now die of infectious diseases.

"In Europe, the emphasis in health promotion was on a more macro or economic approach," says McQueen. "We were generally more interested in the social determinants of health." Back in the United States, he found a greater emphasis was placed on the individual. McQueen says that he has, by nature, a more European bent with respect to public health and has brought his European experience back to his work at the CDC.

"We're beginning to develop more of an interest in ethnic disparities and looking at ways to reduce inequalities in health—by improving access to health care, as well as reducing social inequalities. The document *Healthy People 2010*, published in January 2000, reflects this."

Despite the efforts of the CDC, McQueen thinks the "magic bullet" concept is very much alive and kicking in America. "The hope has always been that a new drug or particular approach will win out," he says. "Americans would like to think that the world is not as complex as it is."

At the National Center for Chronic Disease Prevention and Health Promotion, McQueen pursues the CDC's role in global health, while also concentrating on national health care issues related to public health. "We're pushing the role of prevention in health care organizations," he says. "And they're beginning to take it seriously."

McQueen is interested in working with agencies with worldwide infrastructures, such as the World Health Organization, especially when it comes to chronic disease surveillance. But he doesn't like the word "surveillance." He thinks it has a negative connotation, reminiscent of old-style eastern European politics. Monitoring is too passive, however, because it implies watching, without doing anything.

"We're lucky because through the CDC, I think the United States has a sound infrastructure for collecting data and also acting on it," he says. Britain and Europe do not fare as well, in his view. Communicable disease surveillance is better than chronic disease surveillance, but generally Europeans could be doing much better. "There's a tendency to produce perfect data but to do little with it," he says.

The CDC can provide technical assistance to other countries to help them to develop such infrastructure if they want it. Some poorer countries have better systems than the wealthier ones, as a result of colonial legacies; others, such as China, already have systems in place that are working reasonably well because many of their epidemiologists and statisticians have been partly educated in the United States and Europe. China is also willing to spend money on maintaining its systems.

By taking a global approach, the CDC thinks that it can obviate many of the political and historical barriers that tend to appear when an international approach is taken. "Globalization has helped us to reach new places over the past 20 years," says McQueen.

Centers for Disease Control and Prevention, Atlanta, GA

David McQueen thinks it's time to look at health inequalities

At the end of the day, however, the CDC is still a domestic agency, and local health promotion is arguably more important to his work than is global health care. "To be effective in promotional work, you have to collect smaller and smaller units of data," says McQueen. "People want it by the street, rather than the state, before they'll engage in health promotion programs that seek to change behavior." They also have to buy into the notion of self-care, rather than trust in magic bullets.

It can be a long lag time before you see any results, he says, and there is little opportunity for instant gratification in this line of work. "I have pessimistic days, when watching the 2 'tribes' of Northern Ireland trying to live together, and more optimistic days, when I find myself thinking that taking a global perspective might actually be a way to avoid war," he says.

He says that he has a sense of urgency—that the time is ripe to get things done—tempered by a belief that solutions take time.

"The quick-fix approach is a bit suspect," he says. "We've got to accept that we may not see the fruits of our labor in our lifetime, and we have to be happy with small incremental changes and acknowledge that some of our successes are left unseen, such as successful immunization programs."

But, he says, "It's frustrating that we can buy Coca-Cola and McDonald's hamburgers anywhere in the world, but not get fresh drinking water." These companies have clearly established a more successful cold chain than anyone has so far managed for getting vaccines around the world.

Study explores Internet as a tool for care of diabetic patients

Scott Gottlieb, New York

A new study involving patients with diabetes in the United States will show doctors whether it can be beneficial and affordable to use the Internet to make high-tech house calls.

Upstate Medical Center in Syracuse, New York, and Columbia University in New York City will use a $28 million federal grant to deliver health care through the Internet into the homes of 750 rural and inner-city diabetic patients over the next 4 years.

The grant from the US Health Care Financing Administration will provide patients with free personal computers with programming based on Microsoft Windows, access to the Internet, and health monitoring equipment.

The study will recruit 1,500 patients from New York. One half of this group of patients will receive the computers and diagnostic equipment, and the other half will continue with only the usual care from their doctors. The project includes a control group so that doctors can compare health care costs and benefits in the two groups.

"Up front, obviously telemedicine is going to cost more than normal care," said Ruth Weinstock, Director of the State University of New York's Joslin Center for Diabetes in Syracuse. "You have to compare that to the cost of renal failure, and going on dialysis, or the cost of having a stroke, or going blind. We hope to prevent blindness, strokes, and heart attacks. We hope it's obvious that telemedicine is better in the long run."

She said that telemedicine offers two advantages for patients: comprehensive information from an expanded American Diabetes Association web site, and limitless chances for rural patients to receive treatment. "When the winter comes, and the snow comes, often the patients cannot see their health care providers as often as would be optimal," Weinstock said.

"This way, if their blood sugar is very high, we can see that as soon as it happens and make adjustments. They can get 'visits' as often as necessary."

Under the pilot program, patients with computers will have use of a blood sugar monitoring device, an automatic blood pressure cuff, and a camera hooked up to the computer. The camera will allow doctors to look at patients' skin lesions without requiring patients to leave their homes. Patients will have the equipment for at least 2 years.

After receiving training, patients will check their blood sugar level, blood pressure, and other factors and will enter the data into a secure web site for analysis. Patients will receive information through their computers on how to manage their disease. If a patient's data fall outside an acceptable range, an automatic alert will be sent via the Internet to a doctor or nurse.

"Diabetes, more than most other chronic diseases, requires daily self-management," Weinstock said. "One cannot take a vacation from diabetes. We want to give people greater access to information and offer more timely intervention."

Global News Roundup

African heads of state promise action against malaria

More than 50 African heads of state have pledged to halve the continent's malaria deaths by 2010. The declaration was made at the international summit on malaria in Abuja, Nigeria. The disease causes at least 1 million deaths worldwide, of which 90% are in sub-Saharan Africa. The World Health Organization will work with the heads of state to increase the availability of insecticide-treated bed nets, which reduce infection rates, and of antimalarial drug therapy. Malarial control will require annual donations of $1 billion from industrialized countries.

US spends $2.7 million to prevent spread of West Nile virus

New York City's health department has spent the past few months working to prevent the re-emergence of West Nile virus, which caused 7 deaths and 62 cases of encephalitis in the New York metropolitan area in August 1999. The Centers for Disease Control and Prevention, which has developed standardized laboratory tests for the virus, has given grants totaling $2.7 million to 19 state and local health departments for staff training and operation of these tests.

Drug companies cut HIV drug prices in the developing world

The United Nations has announced that 5 multinational pharmaceutical companies will cut the price of antiretroviral medication in the world's poorest countries. More than 90% of HIV-positive people live in the developing world, and most cannot afford the high cost of HIV drugs. A combination tablet of zidovudine and lamivudine will be cut to $2, which is one fifth of its US price. Peter Piot, director of the United Nations program on HIV/AIDS, welcomed the companies' promises but warned that price cuts alone will not curb the epidemic.

Research does not reflect global disease burden

Less than 10% of the world's research budget is spent on conditions that account for 90% of global disease, according to a report from an international research foundation. The Global Forum for Health Research has called for a reallocation of the estimated $56 billion spent annually on health research by the public and private sectors to improve global health. Professor Adetokunbo Lucas, the forum's chairman, said: "The world's two biggest killer diseases—pneumonia and diarrheal disease—illustrate the extreme mismatch between the disease burden and the funding of research and development. Although these two killers represent about 11% of the total global burden of disease, only about a fifth of 1% of health research funding is spent on them."

Media Watch

Pro-sports medicine from the inside

Brendan Staunton, San Francisco

Dr Warren J Strudwick's practice in downtown Oakland, California, looks much like any other—clean and modern, with half a dozen medical magazines piled up on one side. But Strudwick himself is no everyday physician. As orthopedic surgeon to both the Oakland Raiders football team and basketball's Golden State Warriors, he treats some of the most expensive ligaments in America.

Today, he had an errand to run over at the Raiders' training facility and suggested I come along. On the way, I asked him how football and basketball differ to a treating physician.

"They're very different games, different business," he replied. "Everything about basketball is quicker—and I don't just mean on the court. With up to 4 games a week, the time for recovery from injury is shorter, so you have to get the players back on the boards quicker, and management has to make decisions faster."

Most people would consider football the more hazardous sport, but this season, ironically, the Raiders have mostly escaped injury while the Warriors have lived up to their name.

"Usually in basketball, you just get sprains and overuse injuries like tendonitis, but this year, we've had contact injuries, such as 3 broken noses, which is rare. Across the league, too, there have been broken ankles, broken tibias, dislocated shoulders. It's strange."

Arriving at the Raiders' facility, Strudwick banters cheerfully with the women in the reception area before leading me down to the treatment room. The interior is like any large, well-stocked gym, except for the famous "Pirates" emblem that appears everywhere—even on some rolls of medical bandage tape piled up in a box.

Head trainer Rod Martin stopped briefly for a chat. "He's probably the most important man at the club as far as player fitness is concerned," Strudwick later informed me. "He's like the quarterback of the fitness team."

Martin leads the Raiders' team of 3 fitness coaches who deal with everyday injuries and oversee training sessions. The rest of the team consists of a club physician with overall health responsibility, then Strudwick and another orthopedic surgeon, plus a conditioning coach who looks after each player's year-round fitness.

Today, though, the training rooms were quiet, apart from one of the younger players who was soaking in a far corner tub. Looking around the empty weights room and outside onto the green practice lawn, I tried to imagine the intensity of the regular season.

How did Strudwick become involved in this glamorous, high-profile branch of medicine? "Luck, timing, and also being prepared." He grew up in Washington, DC, and is from a family with strong medical roots going back to his grandfather, who was registered as a physician in North Carolina in 1912. Strudwick studied at the Howard University Medical School, one of the traditional black colleges, and chose orthopedics in his final year.

"At the time there was no such thing as managed care, and I wanted a well-rounded specialty that would involve surgery and the chance to work with active people—people who would get well. Oh, and I also wanted to make some cash!"

His interest in the knee grew out of adversity. As a teenager, he suffered from Osgood-Schlatter disease, where excessive repetitive traction on the attachment site of the patellar tendon leads to inflammation and swelling. It was serious enough to require a cast, and the whole episode left a strong impression. After finishing his residency program, he took a 6-month fellowship in St Etienne, France, working with 2 protégés of renowned French knee specialist, Trillaut.

Once established in his own practice, he was contacted by a former junior high school coach to ask if he could work with the USA track and field team. His real break came, however, when the Raiders returned to Oakland and he was approached to join their medical team. It was his first professional sports experience, and he has been retained by the club as a consultant ever since.

David Phillip/AP Photo

I asked if he found it stressful operating on such high-profile sports performers. "Yes," he admitted with an ironic smile, "but you try to treat elite athletes just like you'd treat anyone else. If you're providing uniformly excellent care to all your patients, then that should be fine for your athletes."

However, there are certain special considerations, the biggest of which is the issue of returning to play. Numerous competing interests are involved, from the club's management to the player's agent and family right back to some high school coach whom the player might trust. All of these people have their favorite doctors, and there's large amounts of money involved, so it is not surprising that players are so often advised to go outside the club for second opinions or, sometimes, even for treatment. So how does Strudwick deal with all this interference?

"The most important issue is healing the player's injury. That's number one. Compared with that, all other issues are peripheral, although sometimes they do influence the type of treatment a player gets. Obviously you have to believe you're providing optimal

health care for the players, but you also have to leave them the option to seek outside advice if they wish. Recently, for example, it was a player's parents who advised him to seek a second opinion. People are very savvy about health matters these days, so you really need to accept that and leave your ego at the door."

I asked if these outside opinions ever conflicted with his own. "Usually they don't," he replied. "But if they do, then the player has to make a choice. That's it."

Strudwick works in a prominent area of medicine, in which it would be easy to become egotistic, yet he stresses the value of humility. "I'm not sure everyone feels the need to subsume their ego as much as I do. I'm relatively young, but it really is my preference. Obviously, you need some ego to do this job, but I prefer not to let my decisions dictate my happiness."

The media can also create problems, especially when the complexities of certain injuries are whittled down into neat sports news headlines. Fans can get the wrong idea. "Sometimes, they think the player's lazy or doesn't want to return, but it's usually not true."

A key element of his work is to document all injuries, the first step in understanding causation and implementing prevention strategies. "Any research I do," he said, "is clinically based—developing protocols on how and where injuries occur and how they've been looked after in the past. It's an ongoing aspect of our clinical practice that guides us where treatment is concerned. For example, one year, the Raiders might have a lot of knee injuries. Why did these occur? Maybe we weren't in the type of preseason shape that we could have been."

As part of the medical team, Strudwick attends every Raiders' and Warriors' games that are played at home, which can prove busy when the seasons overlap. He admits to getting emotional about the games, but does he ever experience frustration working with all these young, rich guys?

"These are ordinary people with extraordinary skills and physiology. Apart from that, they have the same weaknesses as other people and the same strengths. You get a wide range of personalities."

Sport has been a big part of his life. As a youth, he played "tackle" football, then water polo and track at school, and he still finds time for the odd game of basketball, just for fun. He has few regrets about his career choice, although the paperwork is growing and the pay could be better. "Each day offers new possibilities. You're involved with young, active people, and you get to see your results in an active way. . . . Sports and medicine—it's a great combination."

A book that disturbed me

Bioethics: An Anthology Helga Kuhse, Peter Singer, eds. Blackwell Publishers, $39.95, pp 600, ISBN 0 631 20311 7

Peter Singer was a keynote speaker at the last annual meeting of the American Society of Bioethics and Humanities in Philadelphia. For various reasons, I had chosen this moment in the program to duck out of the conference. I was completely unprepared for what greeted me as I left the hotel—protesters, many confined to wheelchairs, chanting "Less debate, more hate." This, I discovered, was the disability activist group Not Dead Yet, which is incensed about Singer's stance that some people with disabilities are not "persons" and may be killed or allowed to die with impunity. It is rare for philosophers to incite the ire of the community at large. Socrates and Bertrand Russell did, and now it seems Peter Singer has joined the ranks of infamy.

I am disappointed by Kuhse and Singer's edited collection of philosophical papers on bioethics. The selection is deeply conservative, and it eschews literature at the margins of bioethics. This is a shame because contemplation of narrative ethics, anthropology, families, and communities is where the action has been in bioethics during the past decade. My attention was naturally drawn to the four essays by Singer himself in the volume. Here, I was not disappointed but offended. Singer variously concludes that experimenting on a human embryo is preferable to doing so on a mouse; that chimpanzees are properly called "people," but humans with profound cognitive impairments are not; and that the heart of a handicapped newborn human might be legitimately excised to save a baboon in need of a new heart. Some have argued that Singer is not responsible for these absurd conclusions since he is merely working through the logical outcomes of a particular moral theory, utilitarianism. Whatever faults we may find with the outcome are properly attributed to the theory and not the philosopher. I disagree: Singer is culpable for these views because doing ethics responsibly involves more than logical reasoning alone. Moral intuition acts as an important check on ethical reasoning, telling us that at times it is the theory, not our actions, that must be changed. More than once Singer notes, "At first this sounds crazy," and more than once he fails for not paying attention to his own intuition.

My reaction to Singer's work is akin to discovering that a friend has served me her pet for dinner. As my initial reaction of disgust fades, I would wonder whether the animal was really a pet, and, if it was, whether my friend actually understands what it means to have a pet. Having a pet implies a set of rules describing the proper relationship between owner and pet and not eating one's pet is high on the list. The terms "person" and "animal" come with their own sets of rules, embedded deep within our society, defining relationships among human beings and between people and animals. Singer, in suggesting that these terms or the rules associated with them may be interchangeable, demonstrates the he fails to understand the concepts of "person" and "animal" at all.

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Mail

Pregnancy saves lives

To the Editor,

In his March 2000 Op-Ed piece, David Grimes repeatedly compares pregnancy to a fire that must be extinguished.[1] Surely it follows that women who never become pregnant must have less risk from the worst "fire": cancer. But childless women have about a 90% higher relative risk of contracting breast cancer than women with a first birth before age 20.[2] Nulliparous women also have about double the risk of ovarian cancer compared with parous women.[3] However, in the short term (about 21 months), it is presumed that the mortality risk is higher for pregnant women than nonpregnant women. In May 1985, Dr Grimes and colleagues provided the raw data to disprove the myth that pregnancy has a higher mortality risk.[4] This study involved more than 16 million pregnancies in the United States.

The No. 1 killer of young people between the ages of 15 and 24 is car crashes, which should surprise no one. Are pregnant women much less likely to die in car crashes than nonpregnant women? Yes, more than 80% less likely. Consider the period 1974 to 1978, when about 16,200,000 US women had live births.[4] An extremely low 41 currently or recently pregnant women died in traffic accidents during that period.[4] A top 10 killer of young people is suicides. The Grimes article reports a very low 15 suicides for more than 16 million live births.[4] So, it is clear: pregnancy saves lives. The reduced car crash death risk saves about 8 to 12 lives per 100,000 per year: "Deaths that occurred within one year of the end of pregnancy and were caused or contributed to by pregnancy were classified as maternal."[4] From the data on page 607,[4] the mortality rates can be easily computed (table).

These mortality rates are all lower than those for nonpregnant women. Thus, a proper analogy would be that a full-term birth is like a fire-retardant that much reduces the odds of those terrible "fires": cancer, auto deaths, suicides, etc. As the great epidemiologist Dr Brian MacMahon at Harvard has clearly stated, only full-term births are breast cancer protective.[5]

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Author's response

To the Editor,

Without commenting on the statistical assumptions used by Richmond in his table, I would agree with him that pregnancy confers some important health benefits as well as risks. However, as I have pointed out elsewhere,[1] having a baby is not a pragmatic way to reduce one's risk of cancer, especially for an adolescent. Few will intentionally become pregnant while in high school to lower their

Table *Mortality rates in relation to live births*

All-cause mortality	Car crash death	Suicide	Neoplasm (cancer)	Homicide
15.3	0.25	0.09	0.15	0.05

All numbers are rates per 100,000 live births per year; the rates are based on dividing by 12 months instead of 21 months; that is, the rates are overstated.

risk of ovarian cancer decades later in life. By mimicking the hormonal milieu of pregnancy, oral contraceptives allow women to enjoy some of the health benefits of pregnancy. For example, wide use of oral contraceptives by women in the United Kingdom has been associated with declining rates of ovarian cancer, despite trends toward later first births and lower total parity.[2]

Our goal should be to help women have healthy pregnancies when they desire them. As I pointed out in my Op-Ed piece, emergency contraception has an important role to play when primary contraception fails or is not used.

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Analgesia in patients with acute abdomen

To the Editor,

We applaud the recent review by Brewster et al[1] that sought to shatter the medical myth that analgesia should be withheld in patients with an acute abdomen in the interest of facilitating accurate and timely diagnosis. Patients with abdominal pain from various causes have long been denied the relief from suffering due them because of widespread misconceptions associated with the use of opioids. We have personally given these drugs safely to scores of patients suffering from acute abdominal pain. In doing so, we have applied several caveats that may bear mentioning and are probably deserving of further study.

In evaluating patients with abdominal pain, it is important not to treat all the same. Many discussions consider both abdominal pain and tenderness equally; this grouping is probably not valid. In addition, some discussions consider pain that can be localized to the right upper quadrant, the right lower quadrant, the flank, or the pelvis equal to pain that cannot be localized at all. This can also lead to difficulties, especially if a logical approach to evaluating such patients is not followed. In processes in which inflamed visceral peritoneum is or can be made to come in contact with parietal peritoneum—such as later stage appendicitis, cholecystitis, or salpingitis—treatment with analgesics is likely to reduce or even eliminate the complaint of pain (the very reason the analgesic has been given) but will not completely eliminate localizing physical findings.[2-6] The initial complaint and physical examination will provide guidance as to which patients fall into this group. On the other hand, pathologic processes not characterized by inflammation of the visceral peritoneum, those that are not well localized on examination and that typically produce pain out of proportion to physical findings—including pancreatitis, ischemic bowel, and bowel obstruction—are more likely to be obscured by the administration of opioid analgesics. In such patients, because the physical examination was not useful in the first place, the elimination of subjective complaints can cause difficulties. Although opioids should still be given to such patients, a high index of suspicion must be maintained for disease processes manifest mainly by pain rather than tenderness.

A recent case of which we are aware is illustrative. A middle-aged woman presented to an emergency department with "10 out of 10" epigastric pain, so severe at the outset that she was literally unable to speak to the paramedics who transported her to the hospital. The patient was appropriately treated with intravenous opioid analgesia, and a workup was initiated. At the change of shift several hours later, the oncoming physician noted a moderately elevated amylase level, but the patient was nearly painfree. The physician subsequently canceled an abdominal series that had been ordered and promptly discharged the patient. About 30 hours later, the patient returned in severe pain, hypotensive, and clinically dehydrated. Physical and radiographic examinations revealed dehydration, acidosis, and air-fluid levels, and the patient was discovered during surgery to have extensive bowel necrosis attributable to mesenteric ischemia. Among the mistakes made during the first visit was that once the patient's ability to subjectively sense poorly localized pain was diminished (the therapeutic goal of administering the opioid). it became *more* important than it had been to consider abnormal laboratory findings, perform radiographs, and carefully observe the patient, and this was not done.

The simultaneous goals of achieving analgesia and arriving at an accurate diagnosis are clearly both achievable. However, doing so may require more diagnostic studies and/or more observation time than might otherwise be necessary (such would seem to be the case when treating not only patients with an acute abdomen but also those with blunt abdominal trauma or multiple trauma and head injury). Brewster and colleagues make reference to this in stating that "the traditional teaching of withholding pain medication in patients with acute abdominal pain stems from a time when medicine was without modern diagnostic techniques." Fortunately, we have advanced greatly from that time. Future research should differentiate patients with various presentations of abdominal pain and seek to guide us as to optimal laboratory and imaging studies that should be obtained in conjunction with the administration of analgesic medication.

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Fighting never pays

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QUESTION: A 24-year-old man has a swollen and painful finger (see figure). He states that he was in a fight the night before but does not recall the details because he was intoxicated at the time.

Physical examination shows limited flexion at the proximal interphalangeal joint. No pus can be expressed from the wound on the finger. The patient's temperature is 100.5°F (8°C).

What is the cause of the finger wound, and what are the possible complications of this condition? What is the appropriate treatment?

Swollen and painful finger

ANSWER: The patient sustained a human bite, or clenched fist injury, as a consequence of punching his opponent in the mouth the previous evening. The hand is the most common site for human bite injuries in men. In women, the most common site for such injuries is the breast.

Complications that may result from this type of injury include septic arthritis, osteomyelitis, infection of tendon sheaths, and a persistent infection leading to the need for amputation. It is possible that the patient may not regain full mobility of this proximal interphalangeal joint.

ORGANISMS AND ANTIBIOTICS

The organisms involved in human bite injuries include *Streptococcus* species, *Staphylococcus aureus*, and *Eikenella corrodens*. Amoxicillin/clavulanate (Augmentin) may be started early and given orally for 5 days to prevent an infection. Once the infection is established, intravenous administration of antibiotics is often needed. Gram stain and wound culture help guide the choice of antibiotics, but without knowledge of the organism and its sensitivities, empiric choices include ampicillin/sulbactam or cefoxitin.[1] If the infection does not respond to antibiotics, one should consider involvement by methicillin-resistant *S aureus*.[2] Rabies prophylaxis is not routinely needed in the treatment of human bites.

IMAGING

Plain film radiographs should be obtained to look for a fracture or evidence of osteomyelitis. Because osteomyelitis may escape detection using plain film radiography, a radionuclide bone scan should be considered when the infection does not respond to the initial treatment.

SURGICAL INTERVENTION

Referral to a hand surgeon for consideration of irrigation, debridement, and surgical exploration is appropriate. In a prospective study of 29 human bite injuries caused by the clenched fist, less morbidity was noted in those cases in which the joint was not involved. Early surgical exploration is recommended to identify and treat possible joint injuries.[3]

OTHER TREATMENT METHODS

Hand elevation is an important aspect of treatment of clenched fist injury. During the day, elevation may be accomplished by using a sling. A special splint may be fashioned to keep the hand elevated during sleep.

Because the patient's last tetanus vaccine was over 5 years ago, he was immunized with tetanus/diphtheria toxoids. He did not need tetanus immune globulin because he had had a full primary series of tetanus vaccines as a child.

OUTCOME

The patient was admitted to the hospital, and he responded well to intravenous ampicillin/sulbactam and hand elevation. The plain film radiographs showed no evidence of fracture or infection, and surgical exploration showed no joint involvement. Physical therapy consultation was provided to prescribe range of motion exercises. Despite these efforts, the patient did not regain full mobility of the affected joint.

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Original Research

Mercury poisoning associated with a Mexican beauty cream

ABSTRACT **Objectives** To describe demographic characteristics, patterns of use, and symptoms associated with mercury poisoning among persons who used a Mexican beauty cream containing mercurous chloride and to estimate the prevalence of cream use in Texas near the Mexico border. **Design** Case series and cross-sectional survey. **Setting** Border communities of Arizona, California, New Mexico, and Texas. **Participants** Persons who used the cream and contacted a health department in response to announcements about the cream and households that participated in the Survey of Health and Environmental Conditions in Texas Border Counties and Colonias, 1997. **Main outcome measures** Urine mercury concentrations, self-reported symptoms, and prevalence of cream use among households. **Results** Of 330 cream users who contacted their health department, 96% were women, and 95% were Hispanic. The mean urine mercury concentration was 146.7 µg/L (reference range: 0-20 µg/L). In 5% of 2,194 randomly selected Texas households near the Mexico border, at least 1 person had used "Crema de Belleza-Manning" (Laboratorios Vida Natural, S.A., Tampico, Tamaulipas, Mexico) in the previous year. **Conclusions** Most cream users had increased urine mercury concentrations. Cream use was common in Texas near the Mexico border. Physicians should consider toxicity in patients with neurologic symptoms of unclear cause and use public health departments when investigating unusual illnesses.

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INTRODUCTION

Mercury-containing compounds have historically been used in germicidal soaps,[1] teething powders,[2] medications for psoriasis and syphilis,[3,4] Chinese patent medicines,[5] and skin preparations including skin-lightening creams.[6-8] Mercurial compounds can be absorbed through intact skin.[9,10] Toxic renal,[6,7,11] neurologic,[4,12] and dermal[2,12-14] effects related to the use of topically applied products have been documented in the literature since the early 20th century. Almost all mercury compounds have demonstrated teratogenic effects in animal studies; however, only several compounds have been associated with congenital abnormalities in humans.[15] Because the toxicity of mercurial compounds in skin products far overshadowed their antibacterial and other purported clinical benefits, in 1973, the US Food and Drug Administration banned use of the compounds in over-the-counter skin preparations, except in special circumstances as a preservative in low concentrations (<0.0065%).[16] Mercury-containing skin preparations, however, continue to be unregulated and available in other countries around the world.[1]

BACKGROUND

In November 1995, a San Antonio physician contacted the Texas Department of Health (TDH) and requested assistance in identifying the cause of mercury poisoning in a 15-year-old male adolescent who had no obvious source of exposure. In September 1995, the previously healthy boy, who resided in Texas near the Mexico border, had the onset of fatigue, weakness, insomnia, myalgias of his extremities, severe headache, sore throat, cough, constipation, and paresthesias of his hands and feet. Subsequent problems developed, including the loss of taste, weight loss of about 7 kg (15 lb), and progressive weakness of his arms and legs. A neurologist in Piedras Negras, Mexico, performed electromyelography and measured nerve-conduction velocities, results of which were consistent with a demyelinating polyneuropathy.[17]

In November 1995, the adolescent was evaluated at a hospital in San Antonio, where a magnetic resonance imaging scan of his brain was normal. Findings on examination by a pediatric neurologist included intact cranial nerve function, diffusely decreased deep tendon reflexes, and mild weakness of the lower extremities. The results of a routine heavy metal screen were unremarkable except for a urine mercury concentration of 178 µg/L (reference range: 0-20 µg/L),[18] and chelation therapy with penicillamine was initiated.[17]

The TDH's Office of Border Health conducted an environmental assessment of the adolescent's home in De-

Summary points

- Mercury poisoning has been associated with the use of a mercury-containing beauty cream from Mexico
- The mean urine mercury level among cream users was 146.7 µg/L (reference range 0-20 µg/L).
- Use of the cream is prevalent in border communities
- Physicians should consider mercury toxicity in cases of neurologic symptoms of unclear etiology

cember 1995 and did not detect mercury in paint, soil, or indoor air. Family members reported that they ate fish from Mexico once or twice per year and denied activities at home, school, or work known to be associated with mercury exposure. However, a container of "Crema de Belleza-Manning" that was used regularly by the adolescent for treatment of acne listed calomel (mercurous chloride) as an ingredient. Laboratory analyses indicated that bottles of the beauty cream contained 6% to 10% mercury by weight. The adolescent had been using the cream daily since June 1995 and was advised to discontinue its use immediately.[17,18]

The TDH publicized the dangers of the cream; subsequently, additional cases of mercury poisoning associated with cream use were identified in the United States. This report describes the results of a collaborative investigation among the TDH, the Arizona Department of Health Services, Phoenix; the California Department of Health Services, Berkeley; the New Mexico Department of Health, Santa Fe; the San Diego County Health Department, San Diego, California; and the Centers for Disease Control and Prevention (CDC), Atlanta, Georgia. The objectives of the investigation were to describe demographic characteristics of users of Crema de Belleza-Manning, patterns of cream use, and health problems associated with its use. A previously planned household survey of the Texas-Mexico border area was used to estimate the prevalence of cream use.

PARTICIPANTS AND METHODS

Study population

Public announcements in the 4 border states, issued as early as April 1996, warned the public about the dangers of Crema de Belleza-Manning, told users to stop using the product, and requested that cream users call their local health departments. The public announcements were made through English- and Spanish-language television and radio stations, newspapers, posters, and fliers. Residents of the 4 states who contacted a local or state health department in response to the public announcements and who reported having used Crema de Belleza-Manning were asked to participate in the study. All cream users were advised to stop using the cream immediately and to consult with a physician. In addition, they were instructed how to obtain a urine mercury test and to dispose of leftover cream.

Data collection

Information regarding persons who used the cream was collected through 2 telephone surveys administered in English or Spanish. A few surveys were administered in person at local health offices. The purpose of the initial survey was to assist investigators in rapidly assessing the nature and extent of problems related to cream use; it was conducted between April and October 1996. Information was collected regarding the reason for cream use, frequency and duration of cream use, the location of the cream purchase, the presence of symptoms associated with mercury poisoning, and other possible sources of mercury exposure. The follow-up survey was conducted between October and December 1996, when additional detailed information was collected about patterns of use and symptoms.

Laboratory analysis

Urine specimens were collected at public health clinics, hospitals, and private physicians' offices. Several public and private laboratories analyzed the specimens. Laboratory results either were reported directly to the health department or were requested from cream users' physicians.

Statistical analyses

Data were analyzed using a statistics software program for epidemiology (Epi Info, version 6.1; CDC).

Prevalence of cream use

The Survey of Health and Environmental Conditions in Texas Borders Counties and Colonias, a collaborative effort by the TDH, CDC, and US Environmental Protection Agency, collected cross-sectional data on environmental health conditions from randomly selected households in Cameron, Hidalgo, Webb, El Paso, Maverick, and Val Verde counties, the 6 most populous Texas counties on the Mexico border. In May 1996, 2 questions were added to the survey to determine the prevalence of cream use by households and to determine what proportion of the population had heard announcements about the dangers of the cream. Participants were asked, "Have you or anyone in your household used 'Crema de Belleza-Manning' in the past year?" and "Have you heard any warnings about this cream?" Interviews were conducted in person by bilingual interviewers.

RESULTS

Descriptive study of cream users

A total of 330 cream users contacted 1 of the 4 state health departments. Of the cream users, 317 (96%) were women. Only the women were included in the following analyses. All 317 women (100%) responded to the initial survey, and 204 (64%) responded to the follow-up survey.

Table 1 *Demographic characteristics of women who used "Crema de Belleza-Manning" and who responded to public warnings about the cream in Arizona, California, New Mexico, and Texas, 1995 to 1996*

Characteristics	Women, %
State of residence (n = 317)	
Arizona	45
California	18
New Mexico	15
Texas	22
Age, yr (n = 315)	
<28	34
28-38	33
>38	33
Ethnicity (n = 204)	
Hispanic	95
Non-Hispanic	5
Education (n = 198)	
8 years or less	29
9 years or more	71
Health Insurance (n = 233)	
Yes	61
No	39
Country of cream purchase (n = 215)	
United States	21
Mexico	79

Table 2 *Patterns of Mexican cream use among women in Arizona, California, New Mexico, and Texas, 1995 to 1996*

Variable	Result
Test interval * (n = 203), days, median	58
Duration of use (n = 256), yr, median	4.0
Frequency of use (n = 290),%	
Less than once per day	18
Once per day	30
2-3 times per day	52
Reason for using cream (n = 280), %	
Skin lightener	44
Acne treatment	30
Moisturizer	9

*Number of days between stopping cream use and submitting urine specimen for testing.

Table 1 presents demographic characteristics of female cream users. The median age of cream users was 32 years (range: 14-79 years). Most women purchased the cream in Mexico; however, 21% purchased the cream in the United States, usually at a flea market or herb shop. The patterns of cream use are presented in table 2.

Urine mercury concentrations were measured in 203 (64%) of the 317 women. Because the half-life of inorganic mercury in humans is about 40 days,[19] specimens submitted more than 120 days after the cessation of cream use were considered poor estimates of past concentrations. Of the 150 women who were tested within 120 days of the cessation of cream use, the mean mercury concentration was 146.7 µg/L (median: 79.0 µg/L; range: 0-1,170 µg/L).[20] One hundred twenty-six women (84%) had concentrations of greater than 20 µg/L. For the 53 women (26%) tested more than 120 days after the cessation of cream use, 26 (49%) had urine mercury concentrations above 20 µg/L, and 7 (13%) had concentrations above 100 µg/L.

Cream users self-reported a high prevalence of symptoms associated with mercury poisoning: fatigue (67%), nervousness and/or irritability (63%), severe headaches (61%), insomnia (51%), memory loss (44%), loss of strength in legs (44%), tingling or burning sensations (39%), tremors or shaking of the hands (38%), depression (31%), and a metallic taste in the mouth (20%). Forty-six percent reported having seen a physician for symptoms associated with mercury poisoning.

Fish consumption, a risk factor for exposure to mercury, was infrequent during the 30 days before a urine specimen was submitted. Only 4 women worked in occupations that may have put them at risk for exposure to mercury, 1 as a dentist and 3 as painters.

Prevalence of cream use

In 104 (5%) of the 2,194 households surveyed, at least 1 person reported having used Crema de Belleza-Manning in the past year; 820 (37%) households had heard warnings about the dangers of the cream.

DISCUSSION

We detected high urine mercury concentrations and a high prevalence of symptoms characteristic of mercury poisoning among women who used Crema de Belleza-Manning. Many of the women who used the cream reported seeking medical attention for symptoms characteristic of mercury poisoning. We were aware, however, of only 1 long-time cream user who was diagnosed with mercury poisoning before this study, and no source of mercury exposure was identified in this person until public announcements about Crema de Belleza-Manning were made in April 1996.

Although the results of this study clearly indicate that use of the cream was hazardous, interpretation of the data is limited. The study, which was rapidly conducted to assess the extent and severity of a public health emergency, has 2 primary weaknesses: lack of a nonexposed comparison group, and selection bias. Women who contacted

their health department may have had disproportionately more health problems and symptoms than women who used the cream but chose not to contact their health department. An accurate assessment of exposure was also limited by some women's difficulty recalling and quantifying the volume of cream used and other use patterns. Further, there were no clinical evaluations to objectively measure health problems. An independent study conducted in Arizona, however, included clinical evaluations of 55 persons who used the cream. Although no major abnormalities were found, the urine mercury concentrations of former cream users declined over time from a median of 170 μg/L to 32 μg/L after an average of 139 days.[21] A New Mexico study also found median urine mercury concentrations among 25 users of the cream to be 4 times greater than among controls.[22]

The high urine mercury concentrations clearly confirm exposure to mercury among the women who used the cream. The reported concentrations, however, may not have been precise measurements of mercury excretion because single-void rather than standard 24-hour specimens were collected. Single-void specimens, even those not adjusted for creatinine clearance, have been found to correlate fairly well with 24-hour averages.[23] The additional effects of interlaboratory differences were not evaluated. Overall, however, reported urine mercury concentrations were probably an underestimate of peak concentrations due to the lag time between the cessation of cream use and the collection of a urine specimen. Despite this, more than one fourth of the women tested more than 120 days after the cessation of cream use had urine mercury concentrations above the reference range.

Data from the Survey of Health and Environmental Conditions in Texas Border Counties and Colonias indicated that use of Crema de Belleza-Manning was common, at least in Texas near the Mexico border. Interviews with cream users led to the identification of a second mercury-containing beauty cream produced in Mexico, "Nutrapiel Cremaning," and in April 1997, Canadian health officials issued an alert regarding "Diana Cream," a mercury-containing beauty cream produced in Lebanon.[24] Although these products cannot be legally sold in the United States, this study indicated that Crema de Belleza-Manning was, in fact, available in this country. Most cream users, however, purchased the cream in Mexico and brought it back to the United States. Crema de Belleza-Manning was produced in Mexico since at least 1971 before its dangers were recognized. It is likely that many bottles still sit in bathroom cabinets, along with other mercury-containing products from around the world. Physicians should consider mercury poisoning in any patient presenting with neurologic symptoms of unclear cause and should be reminded to use their health departments to investigate the causes of unusual illnesses. This study highlights the need for continued international standards for the use of mercury in skin preparations.

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COMMENTARY

Unregulated potions still cause mercury poisoning

The toxicity of inorganic mercury, known as the mercuric or mercurous form, has been recognized for centuries. Roman historians noted that men working in Spanish cinnabar mines, rich in red mercuric sulfide, developed tremors, mental deterioration, and ataxia. The idea for Lewis Carroll's mad hatter in *Alice in Wonderland* came from his knowledge of the neural toxicity of mercuric nitrate, which was used in the fur industry to make felt.

Mercurous compounds became the most common form of mercury used in medicinal preparations. They are often regarded as safe and nontoxic, reflected in the innocent names of the preparations, which suggest gentleness and beauty: sweet sublimate, mercurous dulcis, and calomel (from *calos*, meaning "good," and *melas*, "black"). Calomel, or mercurous chloride, probably originated in China and was used by Paracelsian physicians in the 16th century. It was used to treat malaria and yellow fever, and a preparation called "worm chocolate" or "worm candy" was given to patients infested with helminths.[1]

Toxic effects were soon noticed in individuals given large doses for long periods, in whom excessive salivation, gum inflammation, loosening of the teeth, gastrointestinal upset, and an ashen appearance developed. They had troubling neurologic symptoms, such as arm and facial tremors, hyporeflexia, weakness, ataxia, and erethism—unusual timidity and personality change. In 1825, a poem appeared in a Virginia publication warning physicians of the dangers of calomel: "Since Calomel's become their boast,/How many patients have they lost,/How many thousands they make ill,/Of poison, with their calomel."[2(p253)]

Some physicians became alarmed by the toxicity of mercury-containing medicines.[1] In 1822, Samuel Thomson declared that,

> the practice of giving poison as medicine, which is so common among the medical faculty at the present day, is of the utmost importance to the public. . . . and [I] enforce in the strongest manner on their minds the pernicious consequences that have happened and are daily taking place by reason of giving mercury, arsenic, and other deadly poisons to cure diseases.[3]

The toxic potential of calomel was highlighted in 1948. A Cincinnati pediatrician discovered that a common infantile and childhood illness called acrodynia or "pink disease" was caused by the widespread use of calomel in treating childhood teething and constipation.[4] As late as 1950, acrodynia accounted for more than 3% of admissions to children's wards in London hospitals. Official statistics record that 585 children died of pink disease between 1939 and 1948 in England and Wales.

Because of the recognition of mercury's toxicity, compounds containing mercury have been banned from almost all regulated drugs and over-the-counter preparations in the United States and many other countries. But mercury still appears in unregulated potions, as shown by Weldon and colleagues' study.

The authors report a series of patients in whom elevated urinary concentrations of mercury developed, and they had symptoms suggestive of inorganic mercury poisoning, such as tremor and paresthesia. The women had used a cream containing calomel for a prolonged period, and enough mercury had become systemically absorbed to produce a marked rise in urine mercury. Women usually bought the cream in Mexico, although one fifth had obtained it in the United States at flea markets or health shops. Such beauty creams are available worldwide and have been associated with renal and peripheral nerve damage.

Other unregulated potions containing mercury are available in the United States. Kang-Yum and Oransky report the cases of 3 patients who developed inorganic mercury poisoning from Chinese herbal and patent medicines taken orally or as salves.[5] Their article includes a table listing 18 different Chinese patent medicines that contain mercurials.

Physicians should think of mercury intoxication in all patients with unexplained neurologic or cognitive symptoms. Patients who have had access to unregulated products, from either the United States or elsewhere, are most at risk. If the diagnosis is suspected, the patient's mercury levels should be measured and then the suspected product analyzed.

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Pica during pregnancy in low-income women born in Mexico

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ABSTRACT **Objective** To describe pica behavior (ingestion of nonfood items) in pregnant low-income Mexican-born women in Mexico and the United States. **Design** A convenience sample of informants was interviewed with a questionnaire containing open-ended and closed-ended questions. **Setting** A low-income community on the outskirts of Ensenada, Mexico, and clinics serving low-income people in southern California (Santa Ana, Bakersfield, and Los Angeles). **Participants** Of a total of 225 Mexican-born women, 75 (33%) were interviewed in Ensenada, and 150 (67%) were interviewed in southern California. **Results** The prevalence of pica during pregnancy was 44% (n = 33) in the Ensenada group and 31% (n = 46) in the southern California group. Those who reported pica behavior more commonly had a relative who also practiced pica. **Conclusion** The high reported rate of pica in this sample indicates that pregnant Mexican-born women should be screened for pica and educated about the potentially serious effects on the fetus and mother.

BACKGROUND

Pica—the ingestion of nonfood items—has aroused the curiosity of medical personnel since at least the 16th century.[1] Pica in children has been studied extensively, but pica during pregnancy remains understudied and underreported. Recent articles exploring the practice[1-4] have been contradictory and present little conclusive evidence about its cause and prevalence. Pica during pregnancy is a worldwide phenomenon,[5-8] but in the United States it has been studied largely in the South, with an occasional report from the Midwest. Although this behavior is known to occur in pregnant Latina immigrants in the Los Angeles area,[9] there are no detailed descriptions of the practice in Mexican-born women either in the United States or in Mexico.

The prevalence of pica in pregnant women has been reported from as low as 0% to as high as 68% in the various groups studied.[10] In general, pica behavior is probably underreported because the ingestion of nonfood items may be seen as either shameful or merely unimportant and "normal."[4]

Suggested risk factors also vary between studies. A meta-analysis of dirt-, clay-, and starch-eating women found that race was the major risk factor for pica during pregnancy: it was 4 times higher in black women than in white women.[3] A study by Edwards et al,[11] however, found no significant racial difference in the prevalence of pica in a rural obstetric population; instead, a childhood, family, and nonpregnant history of pica behavior played a role. The meta-analysis also indicated that rural women were twice as likely as urban residents to exhibit pica and that lower socioeconomic status, greater maternal age, impaired nutritional status, and a childhood or family history of pica were additional risk factors.[3]

The etiology of pica appears to be complex. Many environmental, nutritional, socioeconomic, physiologic, cultural, and psychiatric causes have been postulated. Some women apparently practice pica for medicinal purposes. For example, clay eaten in parts of Nigeria has been shown to contain kaolinite and to act as a potent antidiarrheal; it binds toxins and bacteria and may form a protective coat on the intestinal epithelium.[8] Culture also can play a role in pica—for example, if it encourages specific dietary practices and indulgence of cravings.[11,12]

Theories concerning possible nutritional deficiencies as a cause of pica are abundant, with many researchers including vitamin and mineral deficiency in the list of suggested risk factors. There are data linking deficiencies with food preferences in animals, but this has never been documented in humans. Dietary differences between women who do and those who do not engage in pica have not been conclusively documented.[3,13] One of the most widely postulated causes of clay and dirt pica is iron-deficiency anemia. The contemporary opinion on mineral deficiency is polarized between Horner and colleagues' view that anemia may be a consequence of pica, rather than a cause,[3] and the more historical

Summary points

- The ingestion of nonfood items (pica) during pregnancy is common in low-income Mexican-born women in both Mexico and the United States
- Items eaten include store-bought substances such as magnesium carbonate as well as dirt and clay
- Substances are chosen because women crave their taste, smell, or texture in the mouth and think that this craving needs to be satisfied
- Health care professionals should screen for this practice because some items ingested, such as tar and laundry bluing, may be harmful
- The fact that pica is so common suggests that women in other ethnic or cultural groups not previously studied may also practice it during pregnancy

evidence that mineral replacement therapy cures pica.[4,15]

Certain items possess a strong sensory attraction for women who practice pica. Edwards et al describe women who liked the odor, taste, or texture of clay and cornstarch.[11] There was a connection between liking the taste of cornstarch and enjoying its texture in the mouth. Cooksey describes a phenomenon of olfactory craving that escalates during pregnancy.[16] Researchers in several countries have reported heightened taste and odor sensitivities in some women during pregnancy.[7,17-19]

The medical consequences, if any, of pica for mother and fetus vary with the nature of the substance ingested.[20,21] Effects on the mother could include dental injury, constipation, intestinal obstruction, dysfunctional labor due to fecal impaction, parasitic infections, toxemia, interference with the absorption of minerals, lead poisoning, and hyperkalemia.[3,9,13] Possible effects on the fetus include prematurity, perinatal mortality, low birth weight, irritability, decreased fetal head circumference, and exposure to chemicals such as lead, pesticides, and herbicides.[3,5]

There have been no detailed studies describing pica in the Latina population. In our practice, we observed that pica was common in Mexican-born pregnant patients.[22] We therefore conducted a study to assess its prevalence.

PARTICIPANTS AND METHODS

We interviewed 225 Mexican-born women in Spanish over a 4-month period during the spring and summer. The study was carried out both in Mexico (n = 75) and in several areas of southern California (n = 150) to ensure that results would be as generalizable as possible and not simply represent a local phenomenon. Specific sites were chosen because outpatient clinics at those sites were affiliated with the authors' universities, and therefore, the patient populations were readily accessible.

In Mexico, women were recruited by systematically visiting all households surrounding a community clinic in a low-income neighborhood on the outskirts of the city of Ensenada, Mexico, which is 75 miles south of the border. In California, subjects were recruited by approaching women consecutively in medical facilities serving low-income populations in the cities of Santa Ana, Bakersfield, and East Los Angeles—all within 250 miles of the border. These were indigent-care facilities where women did not have to pay for care with their own funds. Of the 150 women interviewed in southern California, 102 were interviewed in Santa Ana, 36 in Bakersfield, and 12 in East Los Angeles.

The criteria for participation were that participants had to be Mexican-born, speak Spanish as their primary language, and be pregnant or have been pregnant within the past year. Within these variables, the sample was a convenience sample: all women were interviewed who agreed to be interviewed. Only 5 of those approached declined to participate. The refusal rate was low because the women understood that we were part of a team that had provided good medical treatment to the community for many years.

A questionnaire was composed in Spanish, and the University of California, Irvine, Department of Interpreter Services used standard methods of back-translation to validate its wording. After pilot testing, the final version of the questionnaire included 15 questions. We began by eliciting demographic data through closed-ended questions and then focused on pica behaviors, giving the informants a few examples of nonfood items that women might eat while pregnant and inviting them to supply their own examples in an open-ended manner.

The protocol for the research was reviewed and approved by the institutional review boards of the University of Southern California School of Medicine and the University of California, Irvine, College of Medicine. All participants gave informed consent before the questionnaire was administered. One of us (E S), who is fluent in Spanish, interviewed about half of the women; the others were interviewed by other authors accompanied by native speakers of Spanish so that unimpaired communication could be assured across the sample of women interviewed.

RESULTS

Demographic data

Participants in both Mexico and southern California had a mean age of 25 years (range: 18 through 42 years) and a mean of 7 years of schooling (range: 1 through 10 years). All reported that they were married. All were medically indigent and lacked private health insurance, but during their pregnancies, their medical expenses were covered by government programs in their respective countries. Women had been born in many different regions, but were principally from rural areas of central and southern Mexico.

Prevalence of pica

Of the 75 mothers interviewed in Mexico, 33 (44%) reported pica behavior, as did 46 (31%) of the 150 women interviewed in the United States ($P < 0.05$ [risk ratio 1.43; 95% CI 1.01-2.04]). The prevalence of pica in the US sites was highest in Bakersfield (42% [n = 15]), followed by Santa Ana (29% [n = 30]) and then East Los Angeles (8% [n = 1]).

Specific items ingested are listed in the table. Twenty-five women described strong cravings for traditional pica items such as dirt, which they said they either ignored or assuaged with "safer" replacements like magnesium carbonate. Reasons given for not eating a craved pica substance were similar in Mexico and the United States: that

Items ingested by low-income Mexican-born women who practiced pica during pregnancy in Mexico (33 of 75 women interviewed) and in the United States (46 of 150 women interviewed)

Item	Mexico (n = 33) No. (%)	United States (n = 46) No. (%)
Dirt	7 (21)	11 (24)
Bean stones*	5 (15)	17 (37)
Magnesium carbonate	1 (3)	8 (17)
Ashes	1 (3)	5 (11)
Clay	0	4 (9)
Ice	0	18 (39)
Other†	14 (42)	17 (37)

*See text.
†Including (in Mexico) battery acid, tar, fabric softener, shampoo, soap, starch, thread, paint thinner, laundry bluing, spearment leaves, and bricks; and (in the United States) eggshells, starch, salt, paper, lipstick, pieces of clay pot, and adobe.

it was "dirty" or unsanitary, that it would have an adverse effect on the fetus, and that someone had said not to do so. All women who refrained from eating dirt because it was unclean stated that they would eat "clean" dirt.

The validity of responses was verified in several ways. First, women showed us half-eaten blocks of clay or magnesium carbonate, "bean stones" (little clods of dirt found among unwashed beans), and/or the location of the clay or dirt they preferred. In addition, they described the types and amounts of materials they consumed with a high level of specificity, offering details that would have been difficult to invent. The reports of others, including neighbors and pharmacists who had observed the behavior or supplied the materials, provided further confirmation of the practice.

Sociocultural aspects of pica behavior

All women interviewed had heard of pica. Overall, those who said they engaged in pica during pregnancy were nearly twice as likely to report having a relative who practiced pica (49/79 people; 62% prevalence) as were those who denied engaging in the behavior (47/146 people; 32% prevalence) ($P < 0.001$ [risk ratio 1.93; 95% CI 1.44-2.58]).

Pica practices

As the table shows, the items reportedly ingested varied somewhat between the women in Mexico and those in southern California. Of these items, only ice was said to be routinely eaten outside of pregnancy, and even ice was eaten in much smaller amounts when the women were not pregnant than when they were.

Ice eating was reported only by US women, probably because no one interviewed in Mexico owned a refrigerator (2 had iceboxes); electricity was a recent arrival, and people were very poor. Quantities eaten daily ranged from about 10 ice cubes to a 32-oz cup of ice. Reasons given for eating ice were thirst, to cool down, and enjoyment of its texture. None of the ice-eating women believed that this could harm the fetus. Women who exhibited pica behavior were much more likely to report eating ice if they lived in Bakersfield, which is very hot in the summer (10 of 36 women, or 28%), than if they lived in Santa Ana (8 of 102 women, or 8%) or Los Angeles (0%). If the 12 women who ate only ice were removed from the count, then the percentage of US women who reported engaging in pica behavior would drop from 31% to 23% (34 of 150 women)—lower but still substantial.

In Mexico, women said they ate pica items because of their taste, smell, or texture in the mouth; for medicinal purposes; and (in the case of magnesium carbonate) because of advice from someone. In California, women said they practiced pica because of thirst (ice only); because of the items' taste, smell, or texture in the mouth; for medicinal purposes; because of advice from someone; and for religious reasons. None said they practiced pica to lose weight or increase caloric intake. Medicinal reasons included soothing of nausea, creating a laxative effect (magnesium carbonate), assuaging thirst (ice), and cooling the body (ice). Only 1 woman said she practiced pica for religious reasons. Her mother had told her that consuming a figure of the Virgin of Guadalupe made from holy clay gathered in San Juan de los Lagos, Mexico (figure), would "bring her blessings."

A nearly unanimous theme among those who craved dirt was that its rich smell when freshly watered brought on a strong desire to ingest it. Similarly, women who ate bean stones reported being attracted by the smell of the little clods of dirt they found when washing the beans. In addition, about three quarters of the women said that they felt a yearning for particular substances, such as starch or clay, in the mouth so that they could savor their physical texture. Women who ate magnesium carbonate as a replacement for dirt stated that its texture in their mouth was similar to that of dirt.

Two women volunteered the term "addiction" in reference to their pica. One reported a "withdrawal" consisting of a "fall in blood pressure and sweating" if she did not eat dirt when she craved it. Another woman said that she felt nervous and got the taste of bean stones in her mouth if she did not satisfy her craving for them.

About a quarter of the women believed that practicing pica could harm the fetus—that it could get parasites, a cold, or suffer harmful effects from chemicals in the materials ingested. Many women who thought that pica was harmful continued the practice even after a physician's warning, saying they "couldn't help themselves." Most, however, thought that pica was beneficial for the fetus. Women interviewed in both Mexico and the United States believed that failure to satisfy a pica craving could lead to miscarriage, illness, or a baby "born with its mouth open," which they said meant that the baby would have

unsatisfied needs. Three named benefits of pica, such as "cleansing the baby" (through the laxative action of magnesium carbonate) and making the baby happy.

Women interviewed in Mexico reported various effects of pica on their own bodies, including relief of constipation or diarrhea, depending on amount ingested (magnesium carbonate); skin rash (battery acid); "burned tongue" (paint thinner); and a burning sensation in the stomach (ashes). In contrast, the US women reported only positive consequences of their pica practices: relief of "heartburn" (magnesium carbonate), laxative action (magnesium carbonate), relief of nausea (ice), and cooling of the body (ice).

Magnesium carbonate ingestion

Magnesium carbonate, a pica item not previously described in the literature, plays an important role in the communities studied. On both sides of the US-Mexico border, blocks of white, chalky magnesium carbonate about the size of a 35-mm film box (figure) are sold in pharmacies as a heartburn remedy and as a laxative. Four interviewees said that doctors or nurses in Mexico had recommended eating small amounts to assuage their craving for dirt. The quantity reportedly ingested daily ranged from a quarter of a block to as many as 5 blocks a day.

Women gave many reasons for eating magnesium carbonate: taste, texture in the mouth, medicinal effects, satisfying their craving for dirt, and following someone's advice. Overall, they were not concerned that it would have any adverse effects on the fetus; in fact, as noted earlier, one woman thought it would benefit her baby by clearing out its intestinal tract so it would be "born clean." Effects reported by the women on their own bodies included decreased heartburn, relief of constipation, and diarrhea, the last in a woman who was consuming 4 to 5 blocks a day.

Figure 1 Two common pica items are magnesium carbonate and clay. A. Magnesium carbonate blocks can be obtained at California swap meets and at neighborhood pharmacies and botanicas (herbal medicine shops) in both Mexico and California. B. Small clay blocks from central Mexico stamped with the image of the Virgin of Guadalupe (example shown with watchband) are sometimes brought to the United States.

DISCUSSION

We found a high prevalence of pica behavior in the 2 groups studied. The slightly lower prevalence in the United States—31% versus 44% in Mexico—could be due to lesser availability of clean dirt, clay, and adobe and/or to underreporting of a behavior that is less culturally acceptable in the United States. The observed association between pica activity and having a family member who practiced pica suggests that this may be a learned behavior.

Women who have heightened sensitivity to smell and texture may have a greater tendency towards pica. Knox et al report that Belfast women experiencing heightened olfactory sensitivity during pregnancy had substantially more cravings than did women who noted no change in sense of smell. In addition, pregnant women preferred certain smells.[7] This correlates with Cooksey's findings about the importance of olfaction in pica[16] and is consistent with our own results.

We are concerned that excessive magnesium ingestion could cause harm to the fetus or mother. Reports of a small number of cases have associated the infusion of magnesium sulfate to prevent uterine contractions during the second trimester with impaired formation of fetal bones and hypoplasia of the dental enamel.[23,24] Maternal hypermagnesemia may also occur as a result of magnesium infusion in individuals with already impaired renal function. This in turn may cause depressed maternal respiratory and cardiac rates or decreased fetal heart rate activity.[25-27] Despite the fact that women of Mexican ancestry (and especially those born in Mexico) have generally good birth outcomes,[28] fetal damage from the maternal ingestion of toxic substances may not be evident at birth. It is unclear whether magnesium ingested during pregnancy could produce maternal serum levels high enough to cause fetal or maternal harm, but caution would seem to be in order.

Cultural and family perceptions of the normalcy of pica may influence whether women feel comfortable indulging in cravings and discussing their practice with outsiders, but in the present study, the specific choice of pica item seemed to be driven by individual preference for a

particular texture or flavor, as has been described by Edwards et al elsewhere.[11] Women who ate tar lived next door to women who ate laundry bluing who lived next door to women who ate dirt. At times, however (as with ice), the choice of items was based on availability.

The most commonly reported pica items in Mexico were dirt, bean stones, and magnesium carbonate, whereas dirt ingestion was less common in the United States, with ice and bean stones being the most common pica items. Edwards et al report a similar shift in preferences from clay and dirt in rural environments to ice and freezer frost in urban locations.[13]

Some of the women believed that the failure to satisfy a pica craving could bring harm to them or to the fetus. This idea about bottled-up cravings may also play a role in the withdrawal symptoms—nervousness, sweating, and tasting the substance craved—reported by several women.

The present study shows that in-depth interviews of women can elicit a large amount of information about pica behavior. There is some evidence that self-completed questionnaires are less effective. For example, clinic counselors of the Women, Infants, and Children Supplemental Food Program (WIC) at one interview site reported that their clients rarely checked off "yes" in response to an intake questionnaire item that asked, "Do you eat or crave things like dirt, clay, laundry starch, or freezer frost?" (personal communication). However, many women interviewed at that site admitted to these behaviors when asked about them privately and nonjudgmentally.

Similarly, the fact that only 1 of 12 women questioned at the East Los Angeles interview site reported engaging in pica behavior may be connected with privacy issues. This was the only place where we could not interview women in private, and we noted that they seemed to be embarrassed about discussing pica in front of the onlookers, most of whom were also Latina but born in the United States.

Further research is needed to correlate parity and month of pregnancy with women's pica behavior. Also, additional work should be carried out in a larger number of sites spaced more widely across the United States and Mexico to determine whether the pica beliefs and behaviors documented in this article are widespread. The fact that subjects were born in many different areas of Mexico, however, suggests that pica is common in low-income Mexican-born women.

Pica behavior is probably precipitated by a complex array of factors that we do not fully understand. Until more compelling evidence of its cause makes treatment possible, each woman should be asked about her experience with pica. Health care professionals need to be aware of the high prevalence of this behavior in low-income Mexican-born women and its constantly evolving nature, as evidenced by the emergence of magnesium carbonate as a new pica item. The phenomenon clearly merits further study and increased clinical vigilance.

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COMMENTARY

Pica may be harmful to the fetus and mother

Simpson and colleagues found that 31% of a sample of Mexican-born women living in southern California practiced pica during pregnancy. The prevalence for a sample of women living in Mexico was 44%. Because these samples were not representative, however, these results may not be generalizable to a wider population. Some ingested substances were benign, such as ice. Others were potentially harmful, such as magnesium carbonate, or clearly toxic, such as paint thinner and battery acid. Although pica has been described in other populations, this is the first report describing the practice of pica in these specific communities.

This study is of possible public health importance, particularly in California. Nearly half of all births in this state are to Latinas (47% in 1998), and nearly three quarters of Latinas giving birth in California were born in Mexico and Central America (71% in 1998). Although pica itself has not been implicated, there is a theoretic risk that it may result in maternal and fetal harm. Excessive magnesium carbonate ingestion by a person with impaired renal function, for example, may pose such risks. Elevated magnesium blood concentrations can cause depressed maternal respiratory and cardiac rates or depressed fetal heart rate activity.[1-3] The use of magnesium sulfate infusions in the third trimester of pregnancy for tocolysis has been linked to impaired formation of fetal bones and hypoplasia of the dental enamel.[4,5]

Future studies should ascertain the prevalence of pica in the Latino community more broadly, using representative samples. In particular, the prevalence of pica among other Latino subgroups common to southern California, such as Central and South Americans, should be determined. Furthermore, pica should be studied among those born in the United States as well as Latina women born elsewhere to ascertain if differences exist between these 2 groups. In a recent study of pregnant immigrant and US-born women living in south-central Los Angeles, an area with many resident Latinos, blood lead concentrations among immigrants were significantly higher than among US-born women.[6] The authors implicated the practice of pica as one cause of the higher lead concentrations among the immigrant women. Interestingly, the blood lead concentrations among the immigrant women were inversely correlated with their length of time in the United States.

Other variables that should be studied in association with pica include generational status and acculturation. More detailed studies of the prevalence of pica among Latino subgroups will help target interventions. The prevalence of health-related behaviors, such as smoking,[7] alcohol consumption,[8] and dietary habits,[9] changes from first- to second-generation Latinos. Greater acculturation, meaning greater adoption of US cultural norms, has been linked to a higher prevalence of unhealthy behaviors and worse birth outcomes among Latina women.[10]

Interventions to control pica among Latinos may be hampered by the welfare reforms of 1996, which reduced or eliminated access to care for many immigrants. Legal immigrants are not claiming all the public benefits that they are fully entitled to receive, including Medicaid.[11] Because many health promotion and disease prevention interventions are based in populations enrolled in public programs, interventions to reduce pica may fail to reach these groups.

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Faith, hope, and charity: an in-depth interview study of cancer patients' information needs and information-seeking behavior

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ABSTRACT **Objective** To explore why cancer patients do not want or seek information about their condition beyond that volunteered by their physicians at times during their illness. **Design** Qualitative study based on in-depth interviews. **Setting** Outpatient oncology clinics at a London cancer center. **Participants** 17 patients with cancer diagnosed in previous 6 months. **Main outcome measures** Analysis of patients' narratives to identify key themes and categories. **Results** While all patients wanted basic information on diagnosis and treatment, not all wanted further information at all stages of their illness. Three overarching attitudes to their management of cancer limited patients' desire for and subsequent efforts to obtain further information: faith, hope, and charity. Faith in their doctor's medical expertise precluded the need for patients to seek further information themselves. Hope was essential for patients to carry on with life as normal and could be maintained through silence and avoiding information, especially too detailed or "unsafe" information. Charity to fellow patients, especially those seen as more needy than themselves, was expressed in the recognition that scarce resources—including information and explanations—had to be shared and meant that limited information was accepted as inevitable. **Conclusions** Cancer patients' attitudes to cancer and their strategies for coping with their illness can constrain their wish for information and their efforts to obtain it. In developing recommendations, the government's cancer information strategy should attend to variations in patients' desires for information and the reasons for them.

INTRODUCTION

Over recent years, communication and information have increasingly been considered important in helping people to cope with cancer.[1-6] A diagnosis of cancer may invoke uncertainty, fear, and loss that can be alleviated by information.[7-9] Research has indicated that the majority of cancer patients want to be informed about their illness.[5] It is also recognized, however, that patients vary in how much information they want and that this may change during their illness. These attitudes are reflected in the efforts that patients make to obtain further information or to resist information that is offered to them.[10] In 1980, when he was an oncologist and editor of the *New England Journal of Medicine,* Ingelfinger reported that when he discovered he had cancer, he did not want all available information nor have to face the uncertainties of the different treatment choices offered to him.[11] This hints at the complexity of providing information in oncology; information may be ignored or avoided by patients, regardless of their prior knowledge or occupation.

For those who provide care to cancer patients, the challenge is finding a way of providing information that is appropriate for patients who may benefit from knowing something about their illness and its treatment but may not wish to know everything about it at all times. This challenge is particularly important in light of the government's current commitment to build on the work of the Calman-Hine Expert Advisory Group to improve cancer care.[12] Recent developments include plans for a national cancer information strategy, the details of which have yet to be agreed. It is likely that such an initiative could include "core information packages" for all patients (NHS Information Authority, draft consultation document of cancer information strategy). In light of the move toward more formal provision of information, there is an urgent need to understand the ways that and the reasons why patients may choose not to seek or may resist further information about their cancer. This paper reports the

Summary points

- Although cancer patients want to be informed about their illness, not all patients want extensive information about their condition and treatment at all stages of their illness
- Reasons why patients vary in how much they want to know relates to their strategies for coping with their illness
- Faith in doctors' medical expertise precluded the need for further information
- Hope is considered essential for coping and could be maintained by avoiding potentially negative information
- Charity to fellow patients included recognizing that scarce resources had to be shared

findings of a study that explored patients' reasons for not wanting further information.

PARTICIPANTS AND METHODS

Between November 1998 and February 1999, 3 physicians from a cancer center identified patients whose cancer had been diagnosed in the previous 6 months and who were judged well enough to be interviewed. The first 24 patients who met these criteria were asked to participate in our study. Four of the patients declined (3 men), and 3 others (2 men) were too ill to be interviewed on the day of the appointment. Our study was approved by the ethics committee of the study site.

Sociodemographic data were collected using a brief pre-interview questionnaire. In-depth interviews, focusing on the patients' experiences of information about their illness from first symptoms through to diagnosis and treatment, were carried out in the patient's home or the hospital. Each lasted between 45 and 90 minutes. Interviews were audiotaped, transcribed, and analyzed according to the methods of framework analysis.[13] Developed by a specialist qualitative research unit called Social and Community Planning Research, framework analysis involves a systematic process of "sifting, charting and sorting material according to key issues and themes."[13] Transcripts were read repeatedly to identify the key themes and categories, which were then developed into a framework for coding the body of interview data. Multiple coding by 3 of us (GML, MB, and CM) tested the acceptability and reliability of the designated categories, and the validity of the coding was checked through deviant case analysis.[14]

RESULTS

Sample characteristics

Of the 17 patients who completed the interview, 11 were women and 6 were men; 10 were non-manual workers, 3 were manual workers, and 4 were not classified; and 10 were white British, 5 were white other, and 2 were black British. Their median age was 55 years (range 28 to 79). The primary cancer diagnosed was breast cancer (4 cases), lymphoma (4), non-Hodgkin's lymphoma (2), lung cancer (2), and 1 case each of cancer of the colon, bladder, skin, brain, and liver. Two patients had a history of cancer.

Information about cancer and its treatment

All 17 patients interviewed had wanted basic information about diagnosis, treatment options, and common side effects of treatment. The timing of the desire for this information varied, however, as did the level of detail and content. Six patients had made efforts to obtain as much information as possible, but the remaining 11 patients reported minimal efforts to obtain information additional to that offered by hospital staff. All the interviews revealed a variability in attitude toward further information: patients did not want information about everything all of the time, but, at different times since their diagnosis, had wanted more or less information about particular aspects of their condition and its treatment.

Patients' attitudes toward seeking or accepting further information were based on their attitude to the management of their cancer. Systematic analysis of patient narratives revealed three overarching attitudes associated with a limited desire for and use of further information: faith, hope, and charity. Elements of faith, hope, and charity were present in all transcripts and affected information need and information-seeking behavior differently at different times.

Faith

To differing degrees, patients displayed faith in their doctors, and this contributed to their attitude toward seeking information beyond that volunteered by health professionals in routine interactions. Often such faith reflected an understanding of the complexity and medical uncertainty surrounding cancer and its treatment and ultimately reflected a will to live (see box, quote 1). Belief in the maxim that "doctor knows best" sometimes negated the perceived value of additional information, and patients believed (and some found) that additional information could confuse their situation. Having faith in their doctors' ability to successfully deploy what were often perceived as impressive and modern medical technologies often precluded information seeking.

Faith was clearly linked with the view that medical knowledge was difficult to understand. This was particularly the case among older patients, who, because they felt their knowledge and understanding of medicine was limited, believed that additional searching could be dangerous and exacerbate an already difficult situation (see box, quote 2).

Some who spoke of their faith in their doctors' expertise expressed concern that information seeking might be perceived as transgressing their incumbent role as patient. Being a good patient was construed as "doing as you are told" and being a "good customer," as opposed to knowing a lot and being inquisitive (see box, quote 3). For most patients, this perception of themselves as apparently disempowered was rationalized and placed in a favorable light by relying on and having faith in their doctors' expertise. For most, placing their faith in their doctors' hands was a strategy that could change at a later stage depending on various factors, including the course of the disease and the need to maintain a sense of hope (see box, quote 4).

Faith

1 "I didn't know what to expect with the treatment, I was optimistic. I couldn't even think about how I could do chemotherapy. I prepared my mind for whatever it takes, [to] follow the rules of the experts; they have said that this is what I've go to do to get better, and I've got to—whatever way, shape, or form—get better." (Interview 10: 45-year-old man with lymphoma.)

2 "To be honest, when they said to me it's cancer, I thought I'll put it in their hands now because sometimes it can be a dangerous thing when you start listening and looking. We only have a certain amount of intellect, and we only have a certain amount of education. There is nothing like an ignorant man trying to learn and know every little thing about it. With regards to medicine and the like, the less you know, the better." (Interview 12: 74-year-old man with skin cancer.)

3 "Maybe they don't tell you everything—all the side effects—because they think it will frighten you. But if you read it yourself, they probably think, 'Clever woman,' for finding out. They probably think, 'She should be listening to us.' I don't think they particularly like you bringing up ideas, not that much, not really." (Interview 11: 64-year-old woman with brain cancer.)

4 "I don't want to use information lines and things like that at the moment. I'm working on my principle that ignorance is bliss. I am not denying the situation I am in, but I am not speaking to people like that at the moment, I don't feel I need to. At the moment, I get what I want, but not too much detail. Further down the line, it may change, depending on which way it goes, if it's bad." (Interview 5: 44-year-old man with liver cancer, melanoma of the eye 7 years earlier.)

Hope

A sense of hope pervaded all 17 narratives, and for some this was closely linked to fear. Patients created a facade of hopefulness, often in the most advanced cases (see box, quote 1). Hope was indispensable for survival, and this interacted with information seeking in a complex way. For some, it meant avid searching for information, particularly about alternative treatments, but for others, it meant limited searching for or even avoidance of new information. Immediately after diagnosis, patients needed to be enabled to ask questions and search for information; without basic diagnostic information, attempts to find out additional information were often thwarted (see box, quote 2).

At different times during their illness, patients halted their information seeking because of fearful and contradictory information, often a consequence of genuine medical uncertainties. These periods of self-censorship functioned to preserve hope by avoiding negative information about their illness and in turn helped to manage their fears associated with the potential of a negative outcome (see box, quote 3).

Contradictory information was a source of anxiety for most patients, as it often confused treatment decisions already made. Weighing evidence and deciding on the best course of action was difficult, even with a medical background. Depending on the immediacy of the issue, some patients resolved the conflict of contradictory information by calling on other patients and lay contacts (including medical friends) to judge between conflicting accounts (see box, quotes 3 and 4).

Women patients often valued the knowledge and experience of other cancer patients more than medical information, and this personal experience often proved invaluable for making a decision about treatment. By contrast, the men rarely spoke of relying on the experience of other patients; once they left the outpatient clinic or treatment room, they preferred a policy of "life as normal" in which cancer could be forgotten (at least superficially).

Additional information could exacerbate fear and threaten to undermine patients' hopes. Even basic introductory booklets could be frightening; consequently, some patients truncated their efforts to find out more (see box, quotes 2 and 5). Patients were also aware that literature produced for patients "in general" was not necessarily relevant to every individual, and the difficulty of discerning information germane to their own individual situations was clearly frustrating (see box, quote 6).

To avoid the risk of uncovering information that could threaten their hope, some enlisted the help of others in finding out new material. Not everyone had access to proxy informants, however, and those too fearful to assimilate additional information avoided all information sources. Emotive media coverage of "cancer victims" such as Linda McCartney rendered avoidance difficult at times and for some constituted an unwelcome threat to hope (see box, quote 7).

The expression of hope often entailed presenting a brave face to others, and this could itself make it difficult to talk about or seek information regarding cancer. Getting on with life and maintaining a positive outlook was perceived as the approach to managing illness that was most respected by hospital staff, friends, and family. Asking for information beyond the basic details of the diagnosis and side effects of treatment could undermine patients' positive appearance. The pressure to present a hopeful facade also related to a fear of using up any reserve of sympathy and support from friends and relatives (see box, quote 8).

The pressure to preserve a brave face and the linked pressure to avoid information about the illness was more common among men, who maintained hope through silence. Men in particular preferred not to ask questions of the medical profession, or people in their wider social networks, so as to avoid discussions of disease recurrence and, ultimately, death. Efforts to maintain hope could thus drive out interest in finding out further information.

Hope

1 "Fortunately, I've got the slow-growing one; the counselor drew a diagram for me (shows diagram to GML). So she said there was the tumor there [breast], there's the other one there [lung], and then they found a very small one on the top [brain]. So I could actually feel where everything was, which was good, but then also in the fluid going round the brain and down the spinal cord. The doctor said there are other [treatments] if this one doesn't work, so the way I am looking at it is, it's either going to be good, and I don't know what happens after that, or if it isn't, there are other options. Where there are other options, there is still hope." (Interview 3: 54-year-old woman with primary breast cancer and multiple metastases.)

2 "I found out what I had by reading my notes on the way up to X-ray. A high- or low-grade, T or B cell lymphoma. It's no good anyway, because I don't know the difference. Information is difficult in the beginning because I couldn't look at the relevant bits, so it's better to be told your exact diagnosis as soon as possible, otherwise even general booklets are too scary and too detailed—my boyfriend looks for me." (Interview 2: 28-year-old woman with non-Hodgkin's lymphoma.)

3 "In the end, I got so confused and one woman had such an influence on me that I was moving very fast in the direction of thinking I would have chemotherapy, and I wasn't too keen to get too much input that was going to suggest I shouldn't. I think I consciously censored myself. I didn't look chemotherapy up on the Internet; I just have recently, and it's really shaken me." (Interview 1: 48-year-old woman with breast cancer.)

4 "It's very difficult making treatment decisions because of the contradictory information, and it's very difficult not being a medical person. It was this woman in the end who helped me decide. She didn't try to persuade me, but it was something about the reasons she gave, you know, regretting not doing it in the future if I get cancer again. Secretly, I think I knew I was going to do it [have chemotherapy], and I didn't want to find out too much negative information." (Interview 1: 48-year-old woman with breast cancer.)

5 "The thing with these leaflets—I mean, I did start to read a few— but then when you read them you get information, but I think they give you a bit too much about what it's going to do and where it can go. I know I have it, and that's all I want to know." (Interview 9: 60-year-old man with liver cancer.)

6 "I was trying to find information about what treatments are available and things like that, but I kept on finding that every person is different, so I found that trying to find out the different grades and things was difficult. I don't think you can find an answer actually that will satisfy you . . . . I think I've found my way of coping through God—just pray, pray, pray." (Interview 4: 46-year-old woman with breast cancer.)

7 "Trouble was, I used to buy a newspaper every day in hospital, and every day cancer—always somebody who had bravely died of cancer. I was a bit cross, and I nearly wrote to the [newspaper] because it was every day, and I thought, 'Well, what about all those people who bravely live?' " (Interview 6: 64-year-old woman with non-Hodgkin's lymphoma.)

8 "Friends and family expect you to be depressed and talk about it, but if you're all doom and gloom, people won't want to come near you, and you need people. This is why you tend to switch off a bit and just have a good laugh when people come to see you, because then they'll want to come back to see you." (Interview 3: 54-year-old woman with primary breast cancer and multiple metastases.)

Charity

Even in the face of their adversity, all the patients reported having been influenced by thoughts of others whom they perceived to be worse off or more needy than themselves. As with other health system resources, information—or access to those who could provide it—was seen as a limited resource, rationed among all patients (see box, quote 1).

Frequent references were made to the usefulness of the clinic consultation for getting reassurance, which was vital for maintaining hope, and obtaining help in interpreting additional information from independent sources. Nonetheless, patients expressed concern about taking up too much of their doctors' time when other patients were waiting to be seen in the outpatient clinic (see box, quote 2). These sentiments were more evident among those patients with close friends or family (most of our sample), who perceived patients without such support to be more needy and deserving of information (see box, quote 3).

By making comparisons with others, patients could see that their situation was better than that of others. This favorable comparison, however, could then be seen as weakening their claim for scarce resources and giving precedence to the claim of others.

Some found it easier to accept information obtained by friends and relatives because they had not personally used a scarce resource. Similarly, patients clearly found information easier to accept when it was verbally offered by hospital staff rather than having to ask for additional information themselves. Others, however, pointed to the legitimate needs of their fellow patients in explaining their reluctance to make further demands on the time and resources of doctors and nurses in the clinics.

DISCUSSION

We have investigated an observation commonly made by those who provide care to cancer patients that not all patients want extensive information about their con-

Charity

1 "I got information on home nursing, and they came round, but I stopped them in the end. Not because I didn't want them, but after I started on my chemotherapy, they used to pop around to see how I was, but I seemed to be doing okay . . . so I said to them, it's best to just 'phone me. I said there's probably other people who needed to see them more than me." (Interview 9: 58-year-old man with liver cancer.)

2 "The consultant said, 'Have you got any questions?' and I had, but I felt that there was this huge waiting room filled with people. I had written them down, but I then felt very conscious of the fact that the consultant had this enormous pressure of people outside. There was a lot of talk among the nurses about how many people there were, so I knew I had to rush." (Interview 1: 48-year-old woman with breast cancer.)

3 "I haven't used telephone lines or anything like that. I have support from the family, and there are people who have got nobody at all, so why should I bother them when I've got people that I can call on?" (Interview 12: 74-year-old man with skin cancer.)

dition and treatment at all stages of their illness. Although not based on a statistically representative sample, this study provides insights into the reasons underlying patients not seeking for information at particular times during their illness within 6 months of diagnosis.

Limitations of the study

Qualitative methods often dictate small samples, and personal interviews could skew the sample toward patients who find it easier to talk about their illness. The constraints imposed on the recruitment process by the setting of a busy clinic in a cancer center meant that it would have been impossible to sample purposively. Fortunately, however, the final sample comprised patients with a range of sociodemographic backgrounds, cancer types, and experiences of illness. The similarities between some of our core themes and those found in other studies[10] permits confidence in the validity of our data and analysis of the data.

A longitudinal, prospective study could avoid the limitations of single retrospective interviews. A longitudinal approach could also maximize the ability to explore and map out the fluid and changing nature of patients' orientations to the management of their cancer and their subsequent efforts to obtain (and avoid) additional illness information over time. A survey study to assess the generalizability of some of the key findings from this interview study, in particular the determinants of information preference and access to information, such as gender and age, will be reported at a later date.

Reasons for not seeking information

Our study shows that in our apparently "patient-centered" era, some patients (particularly older patients and men) still adopt a nonparticipatory role in the management of their illness.[1,15,16] In the 1950s, Parsons argued that the nature of the roles of patients derived from the faith placed in doctors' medical expertise.[17] These perceptions still exist and influence patients' need for and seeking of information. Wanting to be seen as a "good customer," trusting what a doctor says, and "ignorance" and the consequent (perceived) inability to assimilate medical information are important reasons for patients' non-use of information. Arguably, older patients would have grown up in an era characterized by "doctor-centered" practice,[18] and this may help to explain the greater use of independent information services by younger patients.[19,20]

Men seemed to be less likely to access additional information services, and the next phase of our research will focus on these sex differences. Men maintained hope through silence and, more generally, "strength in silence" (C Moynihan et al, *Strength in Silence: Men and Cancer,* British Psychosocial Oncology Conference, Royal College of Physicians, London, 1999), and this influenced their desire for information at different times during their illness. The value of hope in the management of chronic illness is well established,[21,22] but our study has shown the complexity of the relationship between hope and a patient's desire for information.[23] Hope and fear are intertwined, and patients oscillate between the desire for more information and the avoidance of new information. Hope might be accomplished and maintained through silence, periods of self-censorship, and not searching for information or searching by proxy, and these strategies enable patients to circumvent negative information about their illness, which poses a constant threat to hope. As Pinder found in her study of Parkinson's disease, "knowledge of what the clinical facts mean is not always the priceless resource other writers [suggest]. Sometimes it is too threatening."[10]

Finally, we found that patients' behavior was influenced by consideration of the needs of other patients. This attitude of charity reflected patients' perceptions of a rationed health service and helped to rationalize their having minimal information. This attitude has received little attention in the context of cancer patients (S Morris, Medical Sociology Conference, York, 1998) and should become an increasingly important consideration as rationing becomes more widely acknowledged.

Patients' preferences for information derives from the coping strategy or attitude they have to managing their cancer. While all patients have the right to information, they will wish to use this right to varying degrees at different times. Health service providers need to continuously assess whether each individual patient wants only

limited information or whether external constraints such as a language barrier, clinic organization, or the attitudes of health professionals deny them access to the information they want.

CONCLUSIONS

The factors affecting patients' uptake of information services are complex. Patient orientations toward faith, hope, and charity may mean, at points on the illness path, that patients may prefer to avoid disease-related information and may choose to not use cancer information services. An understanding of the reasons why patients may want only limited information can help to ensure that the national strategy being developed is flexible and responsive to individual's coping strategies and information choices.

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COMMENTARY

What cancer patients want to know: national strategies and individual needs

Leydon and her colleagues present a provocative analysis of the information needs and information-seeking behavior of 17 cancer patients in a London oncology clinic. Through careful framework analysis of patient interviews, the authors identify 3 themes to explain the common observation that different patients want different amounts of information at different times during their illness. Faith in physician expertise, the threat that bad news can impose on hope, and a sense of charity toward the needs of sicker patients appear to limit these cancer patients' pursuit of information. The authors present their findings in the context of exploring a national health care information strategy for cancer patients.

In helping to better understand the needs of vulnerable patients, this well-done study serves an important function. However, it is a qualitative study of a small number of patients in London, so the generalizability of its conclusions must be questioned. The study's findings may not apply to patients from other demographic backgrounds and to populations outside England.

Information-seeking, hope, and support issues appear to be different for men and women and vary according to the age of the patient. The authors promise an evaluation of sex differences in a forthcoming study. Other demographic issues that should be explored include language, race, ethnicity, economic status, and education level. Other sources of belief and understanding, such as religious faith and social support, are also likely to be important.

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Beyond these demographic issues, the themes of faith, hope, and charity are universal in the physician-patient relationship, and they are important in the care of patients in the United States.

FAITH

Several factors suggest that patients in the United States may be less trusting than those described by Leydon and colleagues. Racial differences in health outcomes and the history of institutional racism in American medicine threaten patient trust.[1] Persistent mistrust may be a legacy of the infamous Tuskegee experiment, conducted from 1920 to 1960, in which African American patients with syphilis were denied effective treatment in order to study the natural history of the disease. In addition, faith assumes a fiduciary relationship between the physician and patient that has been threatened by managed care in this country.[2] Reimbursement arrangements are likely to affect patients' beliefs that their physician not only "knows best" but that he or she is motivated to do the best for them.

HOPE

Patients' feelings of hope may also be different in the United States. Although still profound, the ability of patients in this country to pursue denial as a coping strategy may be less evident than in England. Informed consent practices are a pervasive element of US health care. The Patient Self-Determination Act requires all federally funded US hospitals to inform patients about their rights to make medical decisions. Advance directives are more common in this country than in other industrialized countries.[3] The American tradition of malpractice litigation may also lead US physicians to challenge patient denial. Physicians in the United States are keen to disclose as much medical information to their patients as possible, to reduce the chances of being sued.

The mass media may also influence patient hope. In the United States, the television program "ER" exposes its 35 million weekly American viewers to a huge amount of medical information and misinformation. In 1994-1995, regular viewers of the television shows "ER," "Chicago Hope," and "Rescue 911" witnessed 60 episodes of cardiopulmonary resuscitation with outcomes far more successful than in real life.[4] Such exposure, with its dramatic realism, may lead the public to an unrealistic view of medicine's healing power.

CHARITY

Particularities of the US health care system may leave its patients less charitable than those in London. In the absence of a nationalized health system, a sense of rationing of physician time and resources may not be as salient for American patients. In the United States, patients paying for their health care through salary deductions and "out of pocket" may have a greater sense of entitlement. Charity may have less of a role in a competitive health care marketplace, where patients consider themselves paying customers imbued with powerful consumers' rights.

The work by Leydon and colleagues challenges us to explore both the similarities and the differences in our patients. Whereas a study of 17 patients can demonstrate important common themes, it also reveals powerful individual stories. Isolation is one of the most profound experiences reported by cancer patients. In designing large information systems, we must remember that surfing the Worldwide Web can be a lonely process. One young patient in their study discovered on the way to radiology that she had cancer by reading her medical record. This should never happen. National strategies must be tailored to individual patients by compassionate physicians who are knowledgeable not only about patients in general, but about the particular person seeking solace, guidance, and care.

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A systematic review of treatment of settling problems and night waking in young children

ABSTRACT **Objective** To assess the efficacy of treatment of settling problems and night waking in young children. **Design** A systematic review of randomized controlled trials of interventions. **Setting** Electronic bibliographic databases and references on identified papers, hand searches, and personal contact with specialists. **Subjects** Children aged 5 years or younger who had established settling problems or night waking. **Interventions** Interventions had to be described and a placebo, waiting list, or another intervention needed to have been used as a comparison. Interventions comprised drug trials or nondrug trials. **Main outcome measures** Number of wakes at night, time to settle, or number of nights in which these problems occurred. **Results** Drugs seemed to be effective in treating night waking in the short term, but long-term efficacy was questionable. In contrast, specific behavioral interventions showed both short-term efficacy and possible longer term effects for dealing with settling problems and night waking. **Conclusions** Given the prevalence and persistence of childhood sleep problems and the effects they can have on children and families, treatments that offer long-lasting benefits are more appealing, and these are likely to be behavioral interventions.

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INTRODUCTION

Settling problems and night waking are the most common sleep problems in young children, affecting about 20% of children aged 1 to 3 years and about 10% of children aged 4.5 years.[1-4] Such problems are frequently persistent and are associated with behavioral difficulties.[2,3] They also adversely affect families, being linked with maternal ill health and marital discord.[5]

Sedation is the most frequently used therapy for childhood sleep problems, despite concerns about its effectiveness.[6,7] A wide range of other interventions (usually psychological) are available, however, including behavioral programs guided by a therapist, parent educational groups, and self-help booklets.[8-10] Recent reviews give different advice as to the most effective forms of treatment.[7,11-13] Parents often express dissatisfaction with drugs and some behavioral treatments, such as extinction (leaving the child to cry), which can be distressing and impractical for some parents.[14,15] Both professionals and parents would benefit from a greater understanding of the effectiveness of therapies for childhood sleep problems.

We aimed to assess the evidence of efficacy of therapies for settling problems and night waking in healthy young children by systematically reviewing all randomized controlled trials in this area. We considered settling problems and night waking together because they often coexist,[2] and programs that target one tend to have a beneficial effect on the other.

Summary points

- Settling problems and night waking are both common and can be persistent in young children
- A range of therapies exists for these problems, including various drugs and nondrug interventions (primarily behavioral)
- Drugs are effective in the short term for some children, but behavioral interventions are more likely to be effective in the short term and to have continuing benefit in the longer term
- Of the behavioral interventions, extinction has a more immediate effect, but over a longer period, no single behavioral treatment has yet been identified as being more effective than the others
- Choice of treatment should be based on families' preferences and circumstances, because these will affect their willingness and ability to adhere to the chosen treatment

METHODS

Search protocol

Two of us (L W and P R) independently searched for trials on MEDLINE (1966-September 1998), EMBASE (1980-June 1998), PsychINFO (1974-September 1998), *Biological Abstracts* (1985-June 1998), CINAHL *(Cumulative Index to Nursing and Allied Health)* (1982-September 1998), SIGLE *(System for Information on Grey Literature in Europe)* (1980-June 1998), and the Cochrane database (including the *Cochrane Controlled Trials Register*; issue 2, 1998). The search terms "child," "infant," "toddler," "sleep," "settling," "wake," "treatment," "medication," "therapy," and "intervention" were used, as were the names of authors. No language restrictions were applied. Available abstracts were reviewed, and suitable articles were requested, along with those that we could not judge adequately from the abstract.

This search was supplemented by tracking all references in these articles and those cited in reviews,[7,11-13] books,[16,17] and a personal bibliography as well as hand-searching the *Journal of Child Psychology and Psychiatry* for the past 5 years. To identify additional unpublished and published studies, we contacted authors of identified studies where possible and the current manufacturers of trimeprazine tartrate.

Inclusion criteria

We included: studies of young children (aged 5 and younger) with an established sleep problem, recognized as problematic by their parents or carers—settling problem (refusing or taking a long time to settle at night or tantrums at bedtime) or night waking (waking frequently, waking for long periods, or both); randomized controlled trials only (crossover or parallel design); studies not specifically of children with a learning disability or those with a particular physical or mental health problem; studies that described the intervention package, with placebo, waiting list, or another intervention as control; and studies with outcome measures that included number of night wakes, time to settle, or number of nights in which these problems occurred.

Critical appraisal of methodologic quality

The quality of the trials was assessed independently and in an open (nonblinded) manner by 2 of us (P R and V W), using the criteria of Jadad et al.[18] Disagreements were resolved by discussion. This system considers randomization, blinding, and withdrawals (dropouts) from trials. A higher score indicates greater methodologic rigor. These criteria have high interrater reliability and good criterion-related validity when compared with longer scoring systems.[18] This system, however, only assessed the studies as described by the authors. Additional information was extracted on the number and age range of participants in each trial, the referral source, the sleep problem, the intervention and control procedures, the outcome scores and measures, and measurement times.

RESULTS

Overall, 44 studies were located. Ten of these were thought to meet the inclusion criteria, but 1 could not be appraised fully because it did not contain sufficient detail of the methods. Nine studies were finally included: 4 on drugs,[14,19-21] 4 on behavioral treatments (1 also with a booklet component),[8,10,15,22] and 1 on a general nondirective educational approach (delivered by booklet).[23] It would have been inappropriate to perform a meta-analysis because of the heterogeneity of the subjects, treatments, and outcome measures.

Methodologic quality

There was initial agreement between the assessors 78% of the time. The average quality score of the trials was low (2.1). The mean quality score of the trials of behavioral treatment was lower than the drug trials (1.6 [SD, 0.6] vs 2.8 [1.3]).

Drug trials

Table 1 gives the details of the trials. The drugs used were trimeprazine tartrate and niaprazine. Two trials were of drug only versus placebo—either up to 60 mg or 90 mg.[14,19] Both showed a significantly beneficial effect of drug treatment in the short term ($P<0.01$ and $P<0.001$, respectively). The clinical significance is less clear because in both trials, even the children on active treatment continued to wake at night, and as much as a third did not improve with drugs. The results are less convincing concerning a longer lasting effect. The same 2 studies included a follow-up period.[14,19] In Richman's study, the sleep score dropped marginally from 12.4 at baseline to 10.1 at 6 months' follow-up.[14] A third of the subjects, however, had withdrawn from the study at this stage. In the study by Simonoff and Stores, which had a shorter follow-up, the number of wakes at night was reduced from 2.8 at baseline to 1.6 at 4 weeks' follow-up.[19] Because both studies were of a crossover design, there was no matched untreated group with which to compare these rates.

The 2 other drug trials require separate consideration. Montanari et al[20] compared 2 different drugs for sleep problems and found them broadly comparable, although niaprazine (an antihistamine) was marginally better than chlordesmethyldiazepam for night waking. France et al[21] used trimeprazine as an adjunct to an extinction program (ignoring a child's crying), rather than as the primary treatment. Although trimeprazine (plus extinction) did reduce night waking during the first 10 days of the trial more than placebo (plus extinction), there was no difference between the 2 groups at the end of treatment and at 4 weeks' follow-up.

Nondrug trials

Table 2 details the nondrug trials. Several techniques were used in the studies.

Positive routines

A 20-minute winding-down bedtime routine was established, initially close to the time that the child fell asleep,

Table 1 *Randomized controlled trials of drug treatment of children's sleep problems*

Study	Children, No., and problems	Intervention (dose)	Controls	Outcomes	Results
Richman, 1985[14]	22, aged 12-24 mo, recruited from community survey, with night waking	Trimeprazine tartrate (30-60 mg)	Placebo	Sleep disturbance score (number of night wakes and settling)	12.1 with placebo; 8.6 with treatment ($P < 0.01$)
Simonoff and Stores, 1987[19]	20, aged 12-36 mo, referred for study, with night waking	Trimeprazine (45-90 mg)	Placebo	Night waking (frequency and duration)	2.4 wakes per night with placebo; 1.4 wakes per night with treatment ($P < 0.001$)
France et al, 1991[21]	30, aged 7-27 mo, referred to sleep program with sleep disturbance	Extinction plus trimeprazine (30 mg)	Extinction plus placebo	Night waking (frequency and duration)	Intervention group improved quicker than placebo group ($P < 0.01$); no difference shown in longer term
Montanari et al, 1992[20]	60, aged 1-36 mo, selected from pediatric outpatients, with sleep disturbance	Niaprazine	Chlordesmethyl-diazepam	Night waking (frequency)	Control group: 23 of 26 (88%) improved; intervention group: 26 of 26 (100%) improved (difference not significant)

that was brought forward by 5 to 10 minutes per week to an appropriate bedtime. After the routine was completed, any resistance from the child was dealt with by parents saying "It's time for sleep" and placing the child back in bed if necessary.

Graduated extinction

Parents ignored bedtime tantrums for preset time intervals, the duration of which increased each week. At the end of the interval, parents entered the room, put the child back in bed if necessary, and told child it was time for sleep before leaving the room again after a maximum of 15 seconds.

Scheduled wakes

After the collection of baseline data, parents were instructed to wake their child 15 to 60 minutes before the child usually woke spontaneously and to resettle them to sleep in their usual manner. The number and timing of scheduled wakes were modified on a semiweekly basis, depending on the child's sleep patterns during the previous few nights.

Extinction or systematic ignoring

Parents went to their children when they were first heard to cry, checked that they were not ill, changed diapers in the crib if necessary but did not pick them up, soothe, interact, or feed them in any way. Once reassured that the child was not ill, parents left the room and did not return for the duration of that crying episode. Further crying episodes each night were dealt with in the same way.

Modified extinction

Modified extinction involved ignoring the child for 20 minutes, then checking that the child was not ill, but the parents did not pick up, soothe, interact, or feed the child. Having reassured themselves, parents left the room and returned only after the child had displayed a settling problem or night waking for a further 20 minutes. This 20-minute checking interval was maintained throughout treatment. "Support visits," used in conjunction with modified extinction, consisted of a visit from the therapist every 2 or 3 days during the first 3 weeks of treatment.

Educational booklet

An educational booklet gave parents general information about children's sleep, described the advantages and disadvantages of the range of therapies for children's sleep problems, and emphasized that there was no 1 solution. Supportive visits, used in conjunction with the booklet, consisted of nondirective discussion with an untrained counselor about the child's sleep.

Table 2 *Randomized controlled trials of psychological treatments*

Study	Children, No., and problems	Interventions	Controls	Outcomes	Results
Rickert and Johnson, 1988[15]	33, aged 6-54 mo, recruited through newspaper ads, with night waking	Scheduled wakes or extinction	Sleep diary only	No. of night wakes per week	5 with scheduled wakes; 2 with extinction; 8 with controls; both interventions better than control ($P < 0.05$)
Scott and Richards, 1990[23]	90, aged 1-18 mo, referred for study, with night waking	Boolket and support visits or booklet only	Sleep diary only	No. of night wakes per night	1.7 with both types of intervention; 1.9 with control; no difference between treatment groups or control
Adams and Rickert, 1989[8]	36, aged 18-48 mo, recruited through newspaper ads, with settling problems	Positive routines or graduated extinction	Sleep diary only	No. of bedtime tantrums per week (frequency and duration)	1/wk with both interventions; 3/wk with controls; both interventions better than control ($P < 0.001$)
Pritchard and Appleton, 1988[22]	31, aged 9-42 mo, referred for study, with night waking and settling	Modified extinction program and support visits	Modified extinction program only	No. of night wakes per night	No difference between groups; both showed reduced night waking
Seymour et al, 1989[10]	45, aged 9-60 mo, attenders at family counseling agency with sleep problem	Sleep program (behavioral advice booklet and support) or behavioral advice booklet only	Waiting list	No. of night wakes per week	6.9 with sleep program, 4.9 with booklet only, and 11.7 with control; both interventions better than control ($P <$ 0.05

Sleep program

Sleep programs consisted of an individually tailored behavioral program (using a variety of techniques that were also described in the accompanying booklet) with initially daily support telephone calls that decreased in frequency over time, accompanied by a behavioral advice booklet. The booklet contained advice about the importance of consistent bedtime routines, the need to reward appropriate nighttime behavior, and specific ways of removing parental attention at bedtime or during night wakings.

Results

Both scheduled wakenings and extinction reduced night waking compared with a control group in the trial conducted by Rickert and Johnson.[15] Extinction seemed marginally more effective than scheduled wakenings, although it was unacceptable to some parents. Adams and Rickert found that both positive routines and graduated extinction were effective for settling problems.[8] The outcomes of the 2 treatment groups did not differ significantly, but both compared favorably with the outcome of the control group.

Pritchard and Appleton failed to show any effect of adding additional support (in the form of visits) to their modified extinction program.[22] However, the modified extinction procedure, with or without this support, resulted in large reductions in night waking over the course of the trial. Unfortunately, there was no untreated control group with which to compare the results.

Similarly, Seymour et al found no effect of adding telephone support to their trial of a booklet giving specific advice about behavioral techniques.[10] However, the booklet, with or without the telephone support, showed superior outcome compared with the waiting list. In contrast, the study examining a nondirective educational booklet failed to show any benefit over a control procedure.[23]

Three of the trials provided follow-up data for either 6 weeks[8,15] or 3 months[10] after treatment. All 3 showed that treatment effects had been maintained, although only 2[8,15] were able to compare with a control procedure because the control group in the study by Seymour et al[10] went on to receive the intervention. The effect of positive routines and graduated extinction on settling problems was maintained, with parents continuing the treatments, where necessary, over this time.[8] The effect was similarly maintained by both scheduled wakening and extinction for night waking.[15] There are some methodologic concerns with this longer term follow-up data because no information was given about numbers dropping out of the study during follow-up, and only a small number took part in the trials. The data, however, are suggestive of continuing clinically significant treatment effects for these particular behavioral interventions.

DISCUSSION

Overall, drug treatment seemed to be a comparatively effective short-term measure for some children, but specific behavioral treatments were more likely to have both short- and longer term efficacy.

There seems to be evidence that drugs are effective in the short-term treatment of night waking in young children (particularly trimeprazine, 30-90 mg nightly). Evidence of a long-term effect, however, is only patchy and contradictory, showing that, rather than a cure, it should be viewed as an effective short-term intervention. Perhaps it is particularly useful as a relief for parents before or while embarking on other forms of treatment. The problems of adverse effects, such as daytime drowsiness, raised by France et al,[21] and parental resistance to giving drugs to their child are also important issues.[24]

In contrast, the results show that some nondrug interventions may be effective in both the short term and the longer term. Both a positive routine program and graduated extinction produced a benefit for settling problems compared with no treatment. Extinction and scheduled wakening had a beneficial effect on night waking compared with control groups. Extinction seems to have achieved clinically useful effects more quickly. All these treatments maintained their effectiveness in the longer term (up to 6 weeks), offering an important advantage when compared with the use of drugs. France et al showed no long-term benefit of adding drugs to a behavioral program such as extinction, but noted less night waking initially when it was used.[21] This may increase the acceptability of extinction to some parents and suggests that there may be a role for novel combinations of approaches, not necessarily with a view to increasing efficacy but perhaps addressing issues such as compliance and acceptability to parents.

Specific behavioral advice in a written form, as with conventional delivery guided by a therapist, had a beneficial effect on a night-waking group compared with a waiting-list control group.[10] A nondirective educational approach with a booklet was ineffective, even though the written material was combined with supportive visits from an untrained counselor. This suggests that the content of any advice, rather than the method of delivery, may be the more important predictor of effectiveness.

CONCLUSION

Conclusions drawn from our review should be considered tentative because most trials conducted thus far have been small and the methodologic quality (particularly of the nondrug trials) generally poor. The possibility of a positive publication bias should be considered. The acceptability to parents and children of the various interventions (which would influence compliance and outcome) is not fully addressed by our study. It can be concluded, however, that a variety of treatment options are available to health care professionals when faced with the common problem of childhood sleep problems. Trimeprazine treatment is an effective short-term option, but longer term and probably greater overall benefit is likely to be achieved by the use of psychological treatments. These are the treatment of choice for parents. The lack of an obviously most effective behavioral program or method of delivery shows that further research is necessary to evaluate the various treatments (or combination of treatments) for this common and often distressing problem. Because there is no single psychological treatment more clearly efficacious than the others, the choice of treatment needs to be based on families' preferences and particular circumstances.

The initial part of this study was undertaken by P R and submitted as a requirement for the University of Oxford postgraduate certificate in evidence-based health care. Some of the preliminary data were presented at a meeting of the Royal College of Psychiatrists Faculty of Child and Adolescent Psychiatry in September 1998. We thank Mrs Janet Harris (course director of the Oxford masters program in evidence-based health care) and Ben Thornley for helpful advice and encouragement during the early stages of this work. Contributors: P R and V W conceived the idea for the study, which was developed along with L W and G S. L W and P R undertook the literature searches, and P R and V W critically appraised the studies. P R and L W wrote the initial draft of the manuscript, to which all 4 authors contributed. P R and L W will act as guarantors for the paper.

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COMMENTARY

Challenges in managing sleep problems in young children

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Competing interests:
None declared

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Ramchandani and colleagues have systematically reviewed trials of interventions for the 2 most common sleep concerns in children younger than 5 years: delayed sleep onset and problematic night waking. As the authors note, there is a relative paucity of well-controlled and methodologically sound studies of these interventions. This paucity reflects the difficulties in conducting this type of research, and it leads to difficulty in translating study results to the clinical setting.

Methodologic weaknesses in many of these studies include small sample size, the failure to include a control group, and reliance on subjective parental reporting to assess efficacy. In addition to these flaws in study design, a variety of other factors could have influenced treatment outcome, including individual differences in child temperament, educational level of the parent, and the presence or absence of marital difficulties. It is therefore not surprising that the more "generic" approaches, which failed to include a behavioral program tailored to the individual family or to address potential barriers to compliance with the treatment plan, were generally associated with worse clinical outcomes. In weighing the likelihood of success of any of the treatment methods discussed for an individual patient, the clinician must take these variables into account. In complex cases, referral to a sleep disorders center or a mental health professional is entirely justified.

The use of medication to treat childhood behavioral problems is highly controversial. This review addresses the use of sedative medication to treat sleep problems in young children, either alone or in combination with behavioral management. There is widespread concern that medication is being used inappropriately for treating a wide range of behavioral difficulties in young children. Anecdotal evidence suggests that both over-the-counter and prescription sedatives are commonly used for pediatric sleep problems in the United States, even in infants. For example, in a recent survey of pediatric practitioners in the northeastern United States, we found that over 20% of the practitioners were at least occasionally recommending diphenhydramine (Benadryl) at bedtime as a treatment for night terrors, a practice not based on empirical evidence.[1] Clonidine, an alpha agonist with sedative properties, is used by child psychiatrists for treating delayed sleep onset in children, despite reports of potentially serious and even fatal cardiovascular side effects.[2]

Although the study by Ramchandani and colleagues suggests that the addition of sedative medication at the initiation of a behavioral treatment program might improve outcome, perhaps through improving parental compliance, they found little evidence supporting the use of medication as an isolated method of treatment, especially on a long-term basis. In addition, such treatment practices may implicitly encourage parents to seek out pharmacologic solutions for their child's behavioral problems, instead of instituting a more labor-intensive but ultimately more successful behavior management program.

Finally, it is worth emphasizing that the definitions of sleep onset and night waking problems in young children are, to a certain extent, culturally determined. Our society places a high value on early acquisition of independent skills by children. This promotes the belief that "self-soothing" in infants is an important developmental milestone and that co-sleeping, or sleeping with a parent or sibling, is not an acceptable practice because it prevents the infant from becoming independent. Health care practitioners should be sensitive to potential cultural and individual family differences in the perception of sleep behaviors in children and take these into account in preventive and management strategies.

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Journal Digest

What are the experiences of women with breast cancer as they decide whether to use complementary/alternative medicine?

Boon H, Brown JB, Gavin A, et al. Breast cancer survivors' perceptions of complementary/alternative medicine (CAM): making the decision to use or not to use. *Qual Health Res* 1999;9:639-653

DESIGN
Focus groups.

SETTING
London and Toronto, Ontario, Canada.

PARTICIPANTS
Thirty-six women (ages 41 to 73 years) diagnosed with breast cancer at some time in their lives were recruited through notices to regional support groups, cancer centers, health food stores, and pharmacies. Most were white and middle to upper middle class. They had been diagnosed an average of 5 years before the study (range 8 mo to 15 yr). Eleven women said they were nonusers of CAM; 25 identified themselves as users.

METHODS
Three focus groups were held in each site. During the 2-hour audiotaped discussions, women were asked about their perceptions and experiences regarding their use or nonuse of CAM (use of natural health care products and seeking advice from nonconventional health care professionals). Data collection continued until saturation. Verbatim transcripts were content analyzed independently by 4 of the researchers, analyses were combined, and key emerging themes were confirmed by 2 breast cancer survivors.

MAIN RESULTS
Key themes included the discovery and investigation of CAM, the decision-making process, and barriers to using CAM. After diagnosis, women began a process of discovering CAM through word of mouth, the media, conventional and CAM practitioners, and personal reading. After they discovered CAM, women investigated the treatment by reading the literature and talking with breast cancer survivors and practitioners. The decision to use or not use CAM was an individualized process. Women recognized their personal responsibility for decision making and noted the need for guidance. Some physicians were supportive; others were skeptical or actively discouraged the use of CAM. Women reported that friends and family served as sounding boards and provided emotional and financial support.

Reasons for deciding not to use CAM included inadequate information, a perception that the treatments were not effective, and fear that they could be harmful. Reasons for deciding to use CAM were improved chance of survival, reaction to bad experiences with conventional medicine (such as treatment failure or adverse effects), prevention of further illness (believing CAM could boost the immune system), and belief that they had "nothing to lose" because CAM was not harmful. Barriers to using CAM included the cost of treatment (CAM was usually not covered by government health care plans), lack of access (treatments were not directly accessible or required a physician's order), and the large amount of time required (such as multiple visits to practitioners, adherence to treatment schedules, and preparation of special diets).

CONCLUSIONS
Women with breast cancer went through a process of discovery and investigation when deciding whether to use CAM. Those who decided to use CAM saw potential benefits and no harmful effects; those who decided not to use CAM had explicitly considered the risks.

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Commentary

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This study by Boon et al offers insight into the process women used to make decisions about CAM in a time of increased publicity and attention to CAM treatments. Data were generated in focus groups with a fairly homogeneous group of white middle to upper middle class women. Other demographic information, such as education level or marital status, was not provided. These findings may not apply to women who differ from those included here. The careful process of data collection and analysis, however, strengthens the results.

One important aspect of this study is that all of the participants at least considered CAM as an adjunct to their treatment. The authors developed a model that identifies the complexity of the individual decision-making process. This model may be helpful for those working with breast cancer survivors to understand and support their process of discovery.

We cannot assume that all women with cancer will consider CAM. This study highlights, however, the need for health care professionals to know about CAM practices in order to provide comprehensive and holistic care. Participants who elected not to pursue CAM were presented as mostly having "risk awareness," whereas those who used CAM were identified in part as feeling "that they had nothing to lose." Treatments considered by the participants were mostly those involving ingested substances, such as herbs and other supplements, which indeed might have potential risks. It is important to assist clients in all aspects of their decision making. CAM treatments described as having no inherent risk (such as energy-based therapies) may not fit this model of risk awareness.

Can a school-based intervention to reduce television use decrease adiposity in children in grades 3 and 4?

Robinson TN. Reducing children's television viewing to prevent obesity: a randomized controlled trial. *JAMA* 1999;282:1561–1567

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DESIGN

A 7-month, randomized (allocation concealment*), blinded (outcome assessors and statisticians*), controlled trial.

SETTING

Two public elementary schools in one school district in San Jose, California.

PARTICIPANTS

Of 227 eligible children in grades 3 and 4, 198 had parental consent to participate. 192 children (97%) (mean age 9 yr) completed both the baseline and post-intervention assessments.

INTERVENTION

The 2 schools were matched on sociodemographic and scholastic variables. One school (106 eligible children) was allocated to implement an intervention to reduce media use by limiting access to television sets, budgeting watching or playing time, and more selective use or play. Eighteen lessons (30 to 50 minutes each) were incorporated into the standard curriculum and taught by regular classroom teachers who received special training. The second school (121 eligible children) received the usual curriculum (control group).

MAIN OUTCOME MEASURES

Main outcome was adiposity (body mass index [BMI]) measured at baseline (September 1996) and after the intervention (April 1997). Secondary outcomes included subcutaneous fat (triceps skinfold thickness); body fat distribution (waist-to-hip ratio); child-reported time spent watching television, watching videos, or playing video games; consumption of high-fat foods; frequency of eating breakfast and dinner in front of a television; proportion of time eating a snack during media use; physical activities; and cardiorespiratory fitness (maximal, multistage, 20-m shuttle run test).

Curriculum-based intervention to reduce television use versus usual curriculum among children in grades 3 and 4

Outcomes	Adjusted Change (95% CI)†
Body mass index (kg/m²)	−0.45 (−0.73 to −0.17)
Triceps skinfold thickness (mm)	−1.47 (−2.41 to −0.54)
Waist-to-hip ratio	−0.02 (−0.03 to −0.01)
Television viewing (hr/wk)	−5.53 (−8.64 to −2.42)
Video game use (hr/wk)	−2.54 (−4.48 to −0.60)
Meals in front of television (0–3 pt scale)	−0.54 (−0.98 to −0.12)

†Differences between groups after adjustment for baseline value, age, and sex. Negative values indicate a relative decrease in outcome for the intervention group compared with the control group.

MAIN RESULTS

Analysis was by intention to treat. The BMI, skinfold thickness, waist circumference, and hip circumference increased in both groups (as expected for children of this age). Children in the intervention group, however, had relative decreases in BMI ($P = 0.002$), triceps skinfold thickness ($P = 0.002$), waist-to-hip ratio ($P < 0.001$), television viewing ($P < 0.001$), video game use ($P = 0.01$), and frequency of eating meals in front of a television ($P = 0.01$) compared with children in the control group (table). The groups did not differ for videotape viewing, daily servings of high-fat foods, physical activity levels, or cardiorespiratory fitness.

CONCLUSION

A school-based intervention aimed at reducing television and video game use reduced adiposity in children in grades 3 and 4.

*Information provided by author

Commentary

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Interventions to reduce childhood obesity have met with low levels of interest, probably because of the stigma associated with being different or attending a special class. The idea of a curriculum-based intervention designed to reach *all* students is appealing. The study by Robinson found that children who received a curriculum-based intervention aimed at reducing media use made lifestyle changes that resulted in decreased BMI compared with students who received the usual curriculum.

Study strengths include the randomized, controlled design and adjustment in the analysis to account for cluster randomization. To avoid the possibility of teachers delivering additional interventions to prevent obesity, they were kept blinded to the primary hypothesis of the study (that children exposed to the television reduction intervention would significantly decrease their levels of adiposity). Study weaknesses include limited generalizability (only 2 schools were included) and the short period between the intervention and follow-up (7 mo).

The implications for public health or school boards are important. Given the increase in childhood obesity and the associated risk of continued adiposity into adulthood, perhaps school curricula could incorporate interventions designed to reduce media use.

Having worked with obese children for the past 16 years in a private practice where finances prohibit many children from participating in special programs, I am excited about the idea of classroom-based interventions as a way to reach the masses.

What is the meaning of sexual violence in the lives of women who have been sexually assaulted by men they knew well?

Draucker CB. Knowing what to do: coping with sexual violence by male intimates. *Qual Health Res* 1999;9:588–601

DESIGN AND SETTING

Heideggerian hermeneutics in Northwestern Ohio.

PARTICIPANTS

Ten women older than 18 years of age (range: 19 to 57 years, 8 white, 2 African American) who had been sexually assaulted as adults by men they knew well were recruited by public announcements. Seven women had experienced childhood abuse or neglect, and many had several abusive relationships as adults.

METHODS

Interviews (1 to 3 hours) were held with each woman and began with open-ended questions about the meaning of the experience of sexual violence and how it affected their daily lives. The author and another psychiatric nurse independently reviewed the interview transcripts, prepared written interpretations, and discussed and compared the interpretations. A qualitative research group also reviewed selected transcripts and commented on the emerging themes. Five participants provided comments on a written draft of the author's interpretations.

MAIN RESULTS

Two themes emerged: *dwelling with violence,* reflecting the women's stories of feeling unsettled and unprotected amid the violence in their lives (discussed in another paper[1]), and *knowing what to do,* reflecting women's descriptions of how they intuitively knew how to manage their lives during and after the violence. The latter is the focus of this article.

Women told stories of managing their lives in a violent world by "getting past it" and "carrying on." All participants said that they had to figure things out on their own because they did not receive help from institutions charged with helping them or they wanted to decide for themselves how to deal with the violence. The women gave examples of knowing how to survive a particular assault or a lifetime of violence, attempting to stay safe, and making things better. Surviving a particular assault involved knowing whether to resist or succumb; 1 woman said that women know what to do in the situation and that others should not second-guess a woman's decision to fight or to comply. Surviving a lifetime of violence was, for some, supported by finding "better things to do," such as involvement with music, caring for children, or finding meaningful employment. In attempting to stay safe, women did things differently in their relationships or everyday routines to prevent further violence. Women did things to help themselves "feel better" (such as reading self-help books or writing in a journal); "get better" (such as learning assertiveness); "make a better life" (such as training to secure a job); and "make things better for others" (such as participating in the study).

CONCLUSION

Women who experienced sexual violence by men they knew well had an inherent sense of knowing what to do and managed their lives by engaging in activities that they knew were sensible for them in their circumstances.

1 Draucker CB, Madsen C. Women dwelling with violence. *Image* 1999;31:327–332.

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Commentary

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Women's roles in actively dealing with violence have been undervalued in both lay and professional discourses, where women are often portrayed as victims and their ability overlooked. This study by Draucker adds to the growing literature that attends to and values the perspectives of women who experience violence.

Draucker uses Heideggerian hermeneutics deftly and makes it easily understandable. The method is particularly effective because it offers analysis of both the constraints imposed by the violent worlds in which women live and women's room to maneuver within those constraints.

The women in this study experienced multiple forms and episodes of violence, and several discussed general maltreatment of women. Thus, as Draucker notes the stories reflect ways of dealing with various forms of abuse and, for some, with a "lifetime of violence." The findings are, therefore, less about dealing with a particular sexual assault and more about living in a violent world. The findings may be most reflective of women with multiple experiences of violence or may be widely reflective of women living in violent societies.

Although it is important to emphasize women's ability, such understanding must not overshadow needs for meaningful support, nor absolve professionals of providing support. Having "know-how" did not mean that the women did not need support. In fact, many "figured things out for themselves" after failure of systems to which they turned. Rather than using "all-victim" or "all-agent" approaches,[1] we must counter stereotypes and respect women's acts of struggle, while continuing to support those acts.

The study emphasizes respecting women's know-how and the importance of listening rather than questioning or advising. Awareness of women's inherent sense of how to manage may encourage nurses to work with women collaboratively, without dictating choices.

1 Mahoney MR. Victimization or oppression? Women's lives, violence, and agency. In: Fineman MA, Mykitiuk R, eds. *The Public Nature of Private Violence: The Public Nature of Domestic Abuse.* New York: Routledge, 1994:59–92.

Which antibiotics lead to higher clinical cure rates in adults with acute maxillary sinusitis?

Williams JW Jr, Aguilar C, Makela M, et al. Antimicrobial therapy for acute maxillary sinusitis. *Cochrane Review*, latest version, 26 May 1999. In: the Cochrane Library. Oxford: Update Software [CD-ROM]

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DATA SOURCES

Studies were identified by searching MEDLINE and EMBASE/Excerpta Medica (to October 1998), scanning bibliographies of relevant articles, and contacting pharmaceutical companies and experts in the field.

STUDY SELECTION

Studies were selected if they were randomized controlled trials (RCTs) that compared an antibiotic with placebo or with another type of antibiotic in 30 or more patients. Patients were at least 18 years of age and had a history consistent with acute maxillary sinusitis confirmed by radiography or aspiration.

DATA EXTRACTION

Two or more reviewers independently extracted data on study characteristics; interventions; study duration; length of follow-up; co-interventions; compliance; and clinical, bacteriologic, radiographic, and adverse event outcomes.

MAIN RESULTS

Thirty-two RCTs with 34 comparisons met the inclusion criteria. Treatment duration ranged from 3 to 15 days. Penicillin V, 1,200 to 3,960 mg/day, led to an increase in clinical cure or improvement rates. No difference in clinical cure was seen between the amoxicillin and control groups in 2 heterogeneous RCTs. Newer nonpenicillin antibiotics had the same clinical cure rates as penicillin V or amoxicillin (8 RCTs); macrolides or cephalosporins had the same clinical cure rates as amoxicillin-clavulanate (8 RCTs). Five RCTs that compared tetracyclines with a heterogeneous mix of antibiotics could not be meta-analyzed.

Dropouts caused by adverse effects were fewer for macrolides or cephalosporins than for amoxicillin-clavulanate (9 RCTs).

CONCLUSION

In adults with acute maxillary sinusitis, penicillin V or amoxicillin is more effective than placebo and is as effective as nonpenicillins for achieving clinical cure.

Commentary

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Is this systematic review by Williams and colleagues the definitive work on management of sinusitis (also referred to as rhinosinusitis) that primary care internists have been awaiting?[1] The review, based on cases of sinusitis diagnosed by radiography and bacteriologic tests, has determined that antimicrobial therapy with a course of penicillin or amoxicillin for 7 to 14 days is better than placebo and equal to newer nonpenicillins in management leading to clinical cure. Dropouts caused by adverse effects, however, were more frequent with amoxicillin-clavulanate than with cephalosporin.

Despite the clinical trials being done in mostly otolaryngologic settings with diagnoses based on laboratory tests and radiography (rather than history and physical examinations used predominantly by the primary care physician), the newer generation of antibiotics provides no substantive benefit over penicillin or amoxicillin. The data about the usual organisms present and the cure rates obtained in this review show that no advantage exists for cephalosporins or macrolides over simple penicillins, except somewhat less frequent adverse effects.

The clinician judges clinical cure by noting symptom improvement in 3 to 5 days, with resolution of remaining symptoms by 10 to 14 days. Such additional investigative studies as endoscopy, plain or computed tomography, and bacteriologic cultures are obtained for patients whose clinical course either does not respond to first-line therapy or progresses rapidly, indicating a serious infection or central nervous system complication.[2]

This review does not answer all the questions for physicians who manage patients with rhinosinusitis. However, we now have clear evidence for appropriate selection of commonly used effective antimicrobial agents for first-line therapy.

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2 Fagnan LJ. Acute sinusitis: a cost-effective approach to diagnosis and treatment. *Am Fam Physician* 1998;58:1795-1802, 1805-1806.

Best Practice

TOPIC IN REVIEW

Plant sterol and stanol margarines and health

A new polyunsaturated margarine with added plant stanols, Benecol, has been introduced in the United States and in several European countries, and a similar margarine (Take Control) with added plant sterols is available in the United States and will be introduced in Europe under the Flora label later this year. These products lower serum concentrations of cholesterol, but they are expensive.[1-14] In the United States, the cost is about $4.00 for a 250-g tub. This article considers quantitatively the health aspects of adding plant sterols and stanols to margarines and other foods.

Summary points

- Plant sterols and stanols reduce the absorption of cholesterol from the gut and so lower serum concentrations of cholesterol
- Plant sterols or stanols that have been esterified to increase their lipid solubility can be incorporated into margarines and other foods
- The 2 g of plant sterol or stanol added to a 25-g daily portion of margarine reduces serum concentrations of low-density-lipoprotein cholesterol by an average of 0.54 mmol/L (21 mg/dL) in people aged 50 to 59, 0.43 mmol/L (17 mg/dL) in those aged 40 to 49, and 0.33 mmol/L (13 mg/dL) in those aged 30 to 39
- A reduction in the risk of heart disease of about 25% would be expected for this reduction in low-density-lipoprotein cholesterol; this is larger than the effect that could be expected to be achieved by people reducing their intake of saturated fat
- The added costs of $120 per person per year will limit consumption; however, if stanols and sterols become cheaper, their introduction into the food chain will make them an important innovation in the primary prevention of heart disease

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METHODS

Randomized trials included in this review were identified by a MEDLINE search using the term "plant sterols." Additional trials were identified from citations in these articles and in review articles. Other trials in children with familial hypercholesterolemia were not included.

PLANT STEROLS AND STANOLS

Sterols are an essential component of cell membranes, and both animals and plants produce them. The sterol ring is common to all sterols; the differences are in the side chain. Cholesterol is exclusively an animal sterol. More than 40 plant sterols (or phytosterols) have been identified, but β-sitosterol (especially), campesterol, and stigmasterol are the most abundant. These 3 sterols are structurally similar to cholesterol: they are all 4-desmethyl sterols (containing no methyl groups at carbon atom 4).

Stanols are saturated sterols (they have no double bonds in the sterol ring). Stanols are less abundant in nature than sterols. Plant stanols are produced by hydrogenating sterols. The term "sterol" is sometimes used as a generic term to include unsaturated sterols and saturated stanols, but it is used here to refer specifically to the unsaturated compounds.

It was recognized in the 1950s that plant sterols lower serum concentrations of cholesterol[15]; they do this by reducing the absorption of cholesterol from the gut by competing for the limited space for cholesterol in mixed micelles (the "packages" in the intestinal lumen that deliver mixtures of lipids for absorption into the mucosal cells).[6,11,16-18] The average consumption of spreads (margarine and butter) is 20 to 25 g per person per day in Europe but a little lower in the United States (15-10 g per person per day). The estimates of effect apply to an average consumption of 25 g per day (an 8-z tub lasting 10 days for 1 person). The fortified margarines contain 2 g of plant sterols or stanols per daily portion. About 0.25 g of plant sterols and 0.3 g of cholesterol occur naturally in the daily diet; the amount of plant sterols consumed daily is twice as much in a vegetarian diet. The added plant sterols or stanols in fortified margarine reduce the absorption of cholesterol in the gut—both dietary and endogenous (that is, excreted in bile)—by about half, from the normal proportion of about half the total cholesterol to one quarter. This reduced absorption lowers serum cholesterol concentrations despite the compensatory increase in cholesterol synthesis that occurs in the liver and other tissues.[6,11] Plant sterols are potentially atherogenic like cholesterol,[19] but atherogenesis does not occur because so little of the plant sterols is absorbed (for example, about 5% of β-sitosterol, 15% of campesterol, and less than 1% of dietary stanols are absorbed).[16]

The use of plant sterols as cholesterol-lowering drugs has been limited: initially the market was small, and later the greater efficacy of the statins was evident. By the 1980s, however, it was recognized that as naturally occurring substances, plant sterols and stanols could be added to foods. Because fats are needed to solubilize sterols, margarines are an ideal vehicle for them, although cream cheese, salad dressing, and yogurt are also used. Esterifi-

cation of the plant sterols and stanols with long-chain fatty acids increases their lipid solubility and facilitates their incorporation into these foods. Benecol was the first fortified margarine, and stanols were added because the evidence suggested that they had greater potential to lower cholesterol than sterols, and the amount absorbed from the gut is negligible.[16,18,20,21]

BENEFITS OF PLANT STEROLS AND STANOLS

The table summarizes the results of randomized double-blind trials in adults that compared the ability of polyunsaturated margarines with and without added plant sterols to lower cholesterol concentrations. The effect of electing trial subjects who had high concentrations of serum cholesterol in some trials was modest, and with the exception of 1 small trial,[13] mean serum concentrations of low-density-lipoprotein (LDL) cholesterol in the control groups ranged from 3.0 to 4.5 mmol/L (116-174 mg/dL) (median, 3.8 mmol/L [147 mg/dL]), close to the age-specific mean found in the western world. The randomized comparisons in 2 trials suggested that there was little difference in the extent to which sterols or stanols lower cholesterol concentrations (although the confidence intervals are consistent with the evidence above that stanols are better).[1,12] The table shows the reduction in LDL cholesterol in each trial; the reductions in total cholesterol concentrations were similar, and there was little change in serum concentrations of high-density-lipoprotein cholesterol or triglyceride.

The figure shows the reduction in concentrations of LDL cholesterol achieved in each trial and the dose of plant sterol or stanol. The reduction in the concentration of LDL cholesterol at each dose significantly increases with age. In each age group, the dose-response relation is continuous up to a dose of about 2 g of plant sterol or stanol per day. At higher doses, no further reduction in concentrations of LDL cholesterol is apparent, confirming the evidence of a plateau identified by earlier nonrandomized studies.[17] At doses of 2 g per day and higher, the average reduction in serum LDL cholesterol concentrations was 0.54 mmol/L (21 mg/dL) (14%; 95% confidence interval, 0.46-0.63 mmol/L) for participants aged 50 to 59,[3,6,8,11] 0.43 mmol/L (17 mg/dL) (9%; 0.37-0.47 mmol/L) in participants aged 40 to 49,[1,4,5,13] and 0.33 mmol/L (13 mg/dL) (11%; 0.25-0.40 mmol/L) for those aged 30 to 39[1,2,5,10]; this trend was statistically significant ($P = 0.005$). At a dose of 2 g per day (the amount added to a 25-g daily portion of fortified margarine), the reduction in LDL-cholesterol concentration is likely to be at least 0.5 mmol/L (20 mg/dL) for those aged 50 to 59 and 0.4 mmol/L (15 mg/dL) for those aged 40 to 49.

Data from observational studies and randomized trials indicate that in people aged 50 to 59, the reduction in LDL-cholesterol concentration of about 0.5 mmol/L would reduce the risk of heart disease by about 25% after about 2 years.[22] In younger people, the proportionate reduction in risk would be similar (the reduction in cholesterol concentrations is smaller, but the association between cholesterol and heart disease is stronger).[22] Trials of 6 different interventions to lower serum cholesterol concentrations have all found a reduction in the incidence of heart disease (these interventions include 4 pharmacologically unrelated drugs, a reduction in dietary saturated fat, and ileal bypass surgery).[22,23] Nothing except a reduction in cholesterol concentration is common to the 6 interventions, and for each intervention, the proportionate reduction in mortality from heart disease is commensurate with the reduction in cholesterol concentration.[17,18] Margarines with plant sterols or stanols thus reduce the risk of heart disease by one quarter: this is the reduction expected from the decrease in serum cholesterol.

This is an impressive result for a dietary change that, price apart, is modest. It is larger than the effect that could be expected if people ate less animal fat. For a person replacing butter with a plant sterol margarine, the reduction in cholesterol concentration would be even greater. Replacing butter with ordinary polyunsaturated margarines lowers total serum and LDL-cholesterol concentrations by about 0.3 mmol/L (12 mg/dL),[24,25] so the overall reduction would be about 0.7 mmol/L (27 mg/dL), or as much as any cholesterol-lowering drug except statins.

EFFICACY IN COMBINATION WITH LOW-FAT DIETS

One nonrandomized study found only a small average reduction in LDL-cholesterol concentrations (0.16 mmol/L [6 mg/dL]) despite that participants took 3 g of plant stanols daily.[26] The participants were on a low-fat and low-cholesterol diet, and the result was interpreted as suggesting that plant sterols were ineffective when dietary fat, dietary cholesterol, or LDL-cholesterol concentrations are low. This is unlikely. In 2 recent randomized trials of stanol margarines in which participants were on low-fat, low-cholesterol diets, the reductions in serum concentrations of LDL cholesterol were similar to those found in other trials in which the intake of dietary fat was higher.[4,9] Plant stanols were equally effective in patients taking statins, who had mean LDL-cholesterol concentrations of only 2.9 mmol/L (112 mg/dL).[6] Other explanations for the discrepancy are more plausible: chance (at the upper confidence interval of the result, an LDL-cholesterol reduction of 0.43 mmol/L is what might be expected) or the fact that the stanol was administered in capsules and not esterified and blended into the fat of a meal. (Sterols administered in capsules may not disperse fully or dissolve in the gut, limiting their ability to reduce the absorption of cholesterol.[9])

Table 1 *Randomized double-blind trials that reported the difference in serum cholesterol concentrations obtained from using polyunsaturated margarines with and without added plant sterols or stanols. Trials were parallel group trials, unless indicated otherwise*

Trial	No. of participants in treatment group/placebo group	Mean age, yr	Duration of trial, wk	Type	Average daily dose, g	Placebo-adjusted reduction in serum LDL cholesterol, mmol/L (95% CI)
Westrate and Meijer[1] (Netherlands)	80*	45	3.5	Stanol	2.7	0.42 (0.33–0.51)
				Sterol	3.2	0.44 (0.35–0.53)
Hendriks et al[2] (Netherlands)	80*	37	3.5	Sterol	0.8	0.20 (0.10–0.31)
				Sterol	1.6	0.26 (0.15–0.36)
				Sterol	3.2	0.30 (0.20–0.41)
Miettinen et al[3] (Helsinki)	51/51	50	52	Stanol	1.8	0.41 (0.29–0.53)
	51/51			Stanol	2.6	0.59 (0.47–0.71)
Hallikainen and Uusitupa[4] (Finland)	38/17	43	8	Stanol	2.3	0.47 (0.24–0.70)
Vanhanen et al[5] (Helsinki)	34/33	46	6	Stanol	3.4†	0.33 (0.15–0.51)
Gylling et al[6] (Helsinki)	22*	51	7	Stanol	3.0	0.53 (0.30–0.76)
Jones et al[7] (Montreal)	22*	35	1.4	Sterol	1.7‡	0.30 (0.21–0.39)
Gylling and Miettinen[8] (Helsinki)	21*	53	5	Stanol	2.4§	0.45 (0.24–0.66)
Jones et al[9] (Montreal)	16/16	about 50	4	Stanol	1.9	0.64 (0.06–1.22)
Niinikoski et al[10] (Finland)	12/12	37	5	Stanol	3.0	0.50 (0.06–0.94)
Gylling and Miettinen[11] (Helsinki)	11*	58	6	Stanol	3.0	0.50 (0.29–0.71)
Miettinen and Vanhanen[12] (Helsinki)	9/8	45	9	Stanol	1.0†	0.28 (0.01–0.55)¶
	7/8			Sterol	0.8†	0.26 (−0.05–0.57)¶
Vanhanen et al[13] (Helsinki)	7/8	47	6	Stanol	0.8†	0.28 (0.0–0.56)¶
				Stanol	2.0†	0.54 (0.23–0.85)
Plat and Mensink[14] (Netherlands)	70/42	33	8	Stanol	4.0	0.36 (0.23–0.49)

LDL = low-density-lipoprotein; CI = confidence interval
*Crossover trial.
†In mayonnaise.
‡In olive oil.
§In butter.
¶Data from these small trials, which tested low doses, are combined in the figure.

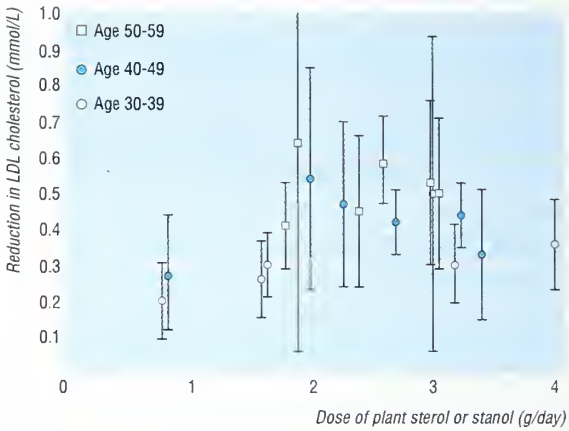
SAFETY

The most important concern about plant sterols is that they reduce the absorption of some fat-soluble vitamins. Randomized trials have shown that plant sterols and stanols lower blood concentrations of β-carotene by about 25%, concentrations of α-carotene by 10%, and concentrations of vitamin E by 8%.[1,2,8,27] Because these vitamins protect LDL cholesterol from oxidation, and sterols and stanols reduce the amount of LDL cholesterol to be protected, the changes in blood concentrations of the vitamins were adjusted in the trials for the lower concentrations of LDL cholesterol. With this adjustment, concentrations of vitamin E were not lower, but concentrations of β carotene were reduced by between 8% and 19%.[1,2,8,27] Randomized trials showed no benefit in increasing the blood concentrations of β-carotene and vitamin E by greater proportions than these,[28,29] although we do not know whether this is the case for other carotenes. Eating more fruit and vegetables would counter the decrease in absorption. The blood concentration of vitamin D is unaffected.[2,8] No other side effects or biochemical anomalies were evident in the randomized trials of plant sterol or stanol margarines (1 of which lasted a year[3]), in earlier studies testing doses as high as 3 g per day for 3 years, or in animal studies testing proportionately higher doses.[16,17,30] Stanol margarines have been sold in Finland for 3 years without evidence of hazard, and a tenth of the amount of plant sterols found in these margarines occurs naturally in a normal diet. Plant sterols or stanols do not adversely affect the taste or consistency of margarines.[3,10]

THE PLACE OF STEROL AND STANOL MARGARINES IN THE DIET

The excess cost per person of margarines containing added plant sterols or stanols is about 33 cents per day, or $120 per year. Affluent people may willingly pay this to reduce their risk of death from heart disease by a quarter, but poorer people, who are at higher risk of heart disease, will tend to be dissuaded from buying the product. The cost reflects the large amount of raw material needed (about 2,500 parts to extract 1 part of sterol). Moreover, supplies are limited. The present sources—a byproduct in the refining of vegetable oils or the oil obtained from pinewood pulp in papermaking—can supply only about 10% of the people in developed countries. In the foreseeable future, the product will be used only by a minority of people. However, in many countries, there is also a legal obstacle: no health claim can be made in the advertising of these margarines because they are a food, not a drug. More people might buy the product if they were aware of the size of the health benefit.

Plant sterol and stanol margarines may appeal to patients with ischemic heart disease, but they should not replace statins because the reduction in the concentration of LDL cholesterol is greater with statins. Both could be taken together, however, because the cholesterol-lowering effects of the 2 are additive.[6] The overall costs of the 2 are equivalent: statins cost about 3 times as much as plant sterol margarines, but they lower serum cholesterol by 3 times as much.



Results of randomized double-blind trials of margarines with and without added plant sterols or stanols showing the reduction in serum concentrations of low-density-lipoprotein (LDL) cholesterol (95% confidence intervals) plotted against the daily dose. The data are from the table.

In the longer term, the addition of plant sterols and stanols to foods could be an important public health policy if new technology and economies of scale can lower the cost and enable a greater demand to be met. The serum cholesterol concentration of the average older adult in western countries is high (5.7-6.0 mmol/L [220-240 mg/dL]), with a correspondingly high lifetime risk of death from heart disease (about 25%). Introducing plant sterols into the food chain would lower the average serum cholesterol concentration in western countries, with the added advantage of "demedicalizing" the reduction (that is, one would not have to become a patient to benefit). There is a precedent for such fortification: in the United States, folic acid has been added to flour since 1997. In addition to the expected reduction in the incidence of neural tube defects, there has also been a significant reduction in the average serum concentration of homocysteine,[31] which is likely to reduce mortality from heart disease.

The launch of margarines containing plant sterols and stanols is a welcome first step in what may become an important innovation in the primary prevention of ischemic heart disease. It is to be hoped that in the longer term, plant sterols and stanols will become cheap and plentiful so that they can be added to foods eaten by most of the population.

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capsule

Drug resistant bacteria cause fresh concern Infections caused by so-called "superbugs," resistant to most available antibiotics, are causing renewed concerns worldwide. Four recent outbreaks of new and more virulent strains of disease caused by contact with animals or contaminated food were reported in the *New England Journal of Medicine* (*N Engl J Med* 2000;342:1280-1281).

capsule

Moderate drinking protects against diabetes US doctors who drink up to 1 unit of alcohol a day could be protecting themselves from type 2 diabetes (*Arch Intern Med* 2000;160:1025-1030). Data from the Physicians Health Study, a cohort of over 20,000 male doctors, shows a clear dose-response relation between alcohol intake of up to 1 drink a day and reduced risk. Note, though, that there weren't enough heavy drinkers in the cohort to study the association beyond moderate drinking.

CLINICAL EVIDENCE

Digestive system disorders: gastroesophageal reflux disease

This article comes from *Clinical Evidence* (1999;1:145-153), a new resource for clinicians produced jointly by the BMJ Publishing Group and the American College of Physicians–American Society of Internal Medicine. *Clinical Evidence* is an extensively peer-reviewed publication that summarizes the best available evidence on the effects of common clinical interventions gleaned from thorough searches and appraisal of the world literature. It became available in the United States late last year. Please see advertisement for more information or, alternatively, visit the web site at www.evidence.org.

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QUESTIONS: What are the effects of treatment of erosive esophagitis? What are the effects of treatment of nonerosive esophagitis? What are the effects of treatment of gastroesophageal reflux disease on the progression of Barrett's esophagus? What are the effects of treatment in people with extraesophageal manifestations of gastroesophageal reflux?

INTERVENTIONS

In descending order of effectiveness

- Proton pump inhibitors
- Histamine-2 antagonists (less effective than proton pump inhibitors)
- Fundoplication
- Medical and surgical treatment of gastroesophageal reflux in selected people with extraesophageal manifestations
- Different surgical therapies for erosive and nonerosive esophagitis
- Medical and surgical treatment of gastroesophageal reflux in people with Barrett's esophagus
- Surgical treatment of nonerosive esophagitis
- Medical and surgical treatment of erosive and nonerosive esophagitis
- Diet and lifestyle changes

DEFINITION

Gastroesophageal reflux occurs when gastric contents enter the esophagus because of transient or chronic relaxation of the lower esophageal sphincter. Excessive reflux causes symptoms of gastroesophageal reflux disease (heartburn, acid taste in the mouth). It can be divided into nonerosive esophagitis and erosive esophagitis in which endoscopy shows inflammation and erosions.

INCIDENCE/PREVALENCE

Gastroesophageal reflux disease is common. Weekly heartburn occurs in about 20% of people questioned in population surveys. As much as 10% of these will have erosive disease.

Summary points

- One systematic review of randomized controlled trials (RCTs) found that proton pump inhibitors were more effective than H_2 antagonists in both erosive and nonerosive esophagitis, and 1 RCT found no significant difference in the effectiveness of different proton pump inhibitors
- We found inadequate evidence from RCTs on surgical treatment versus placebo or versus medical treatment
- We found no RCTs evaluating whether people with Barrett's esophagus benefit from medical or surgical treatment of gastroesophageal reflux
- We found limited and conflicting evidence on the effects of treating gastroesophageal reflux in people with extraesophageal manifestations of gastroesophageal reflux disease

ETIOLOGY

There are no clear predictive factors for gastroesophageal reflux disease.

PROGNOSIS

Gastroesophageal reflux disease is generally benign, with little mortality. Persistent symptoms, however, can interfere with normal activities and cause considerable morbidity. Long-term retrospective data (about 22 years) suggest that, in people with initially normal findings on endoscopy, endoscopic appearance tends to remain normal.[1] In a small subset of people, strictures, Barrett's esophagus, adenocarcinoma, or extraesophageal manifestations develop (table).[2]

AIMS

To relieve symptoms, prevent complications in patients with severe esophagitis, control extraesophageal manifestations, minimize adverse effects of treatment, and improve quality of life.

OUTCOMES

Frequency and severity of symptoms; degree of esophagitis; esophageal pH (assessed by ambulatory monitoring); prevalence and severity of extraesophageal manifestations;

Table *Extraesophageal manifestations of gastroesophageal reflux disease**

Pulmonary	Ear, nose, and throat	Other
Asthma, chronic bronchitis, aspiration pneumonia, sleep apnea, atelectasis, interstitial pulmonary fibrosis	Chronic cough, hoarseness, enamel erosion, halitosis, pharyngitis, subglottic stenosis, vocal cord inflammation, granuloma, possible cancer	Noncardiac chest pain, chronic hiccups, nausea

*From Richter.[2]

and incidence of stricture, Barrett's esophagus, and adenocarcinoma. Symptoms do not correlate well with the extent of esophagitis. People with Barrett's esophagus may have minimal symptoms, and those with severe symptoms may have no evidence of esophagitis.

METHODS

Clinical Evidence issues were searched and appraised through May 1999. Primary sources were searched on MEDLINE, and a manual search was done of earlier issues of *European Journal of Gastroenterology and Hepatology*. Reference lists of retrieved articles were searched.

QUESTION: What are the effects of treatment of erosive esophagitis?

OPTION: PROTON PUMP INHIBITORS VS H_2 ANTAGONISTS

One systematic review of randomized controlled trials (RCTs) found that proton pump inhibitors were more effective than histamine-2 (H_2) antagonists at healing erosive esophagitis and preventing recurrence. No significant difference was found in rates of short-term adverse events. No good data were found on the long-term risks of treatment or on possible long-term benefits.

Benefits

One systematic review published in 1997 identified 43 single- and double-blind RCTs involving 7,635 participants that compared the use of proton pump inhibitors versus that of H_2 antagonists.[3] Proton pump inhibitors were more effective at healing by 12 weeks on endoscopic examination (84%, 95% confidence interval [CI] 79%-88%, vs 52%, 95% CI 47%-57%), irrespective of drug dose or treatment duration. Proton pump inhibitors provided the fastest overall healing rate, with 11.7% of cases of esophagitis healed per week (95% CI 10.7%-12.6%), twice as fast as H_2 antagonists (5.9% healed per week, 95% CI 5.5%-6.3%) and 4 times faster than placebo (2.9% healed per week, 95% CI 2.4%-3.4%). Two of the RCTs added a prokinetic agent to the H_2 antagonist, but results still strongly favored the proton pump inhibitor.[4,5] Doses of proton pump inhibitors varied, not routinely exceeding 40 mg of omeprazole or 30 mg of lansoprazole. In a cohort study of people with esophagitis treated with omeprazole, higher doses achieved even higher healing rates.[6]

Preventing recurrence

Three of the RCTs looked at recurrence rates. Two RCTs (1 double- and 1 single-blind) compared the use of omeprazole versus ranitidine (with or without cisapride) in people with endoscopically confirmed esophagitis who had already received a regimen of omeprazole for 4 to 8 weeks.[7,8] At 1 year, people treated with daily omeprazole were significantly less likely to relapse than those treated with ranitidine hydrochloride. In the first RCT, 159 participants were randomly assigned to treatment with omeprazole, 20 mg daily; omeprazole, 20 mg on 3 consecutive days a week (weekend omeprazole); or ranitidine, 150 mg twice a day. At 12 months, a significantly greater proportion of people treated with omeprazole daily remained in remission than those treated with either weekend omeprazole (absolute risk reduction [ARR] 57%, 95% CI 42%-71%) or ranitidine daily (ARR 64%, 95% CI 50%-78%). There was no significant difference between weekend omeprazole and daily ranitidine treatments (ARR 7%, 95% CI −11% to +25%).[7] In the second RCT, 175 participants were randomly allocated to receive omeprazole, ranitidine, or cisapride alone and in various combinations. After 12 months, people receiving omeprazole were significantly more likely to be in remission than those receiving either ranitidine or cisapride alone (80% still in remission vs 50%; CIs not reported).[8]

Preventing complications

No RCTs that examined possible longer term benefits of medical treatment were found.

Harms

Complications of incomplete treatment

No RCTs were found that examined the course of incompletely treated gastroesophageal reflux disease, nor any

good data on the natural history of inflammatory esophageal disease.[1] Also, no data were found on the level of gastric acid suppression needed to ensure adequate esophageal healing.

Short-term adverse effects

In placebo-controlled RCTs, proton pump inhibitors and H_2 antagonists have similar rates of adverse effects. Most data on significant adverse effects come from case reports or uncontrolled trials. H_2 antagonists have been associated rarely with cytopenia, gynecomastia, abnormal liver function test results, and hypersensitivity reactions. Rare adverse effects of proton pump inhibitors in people with gastroesophageal reflux disease include abnormal results of liver function tests, increased small bowel bacterial counts, cytopenias, hypersensitivity reactions, and decreased (but not clinically important) vitamin B_{12} levels.

Long-term adverse effects

No controlled trials were found with long-term follow-up on the safety of the long-term use of H_2 antagonists. The long-term use of proton pump inhibitors in the presence of *Helicobacter pylori* infection has been linked in 2 uncontrolled trials to atrophic gastritis after 3 to 5 years.[9,10] Among people treated with omeprazole, none of whom had atrophic gastritis at baseline, atrophic gastritis developed in 18 of the 59 people infected with *H pylori* and 2 of the 46 people who were not infected.[9] Of 14 people with persistent *H pylori* infection, 6 developed mild to severe atrophy in 5 years.[10]

OPTION: DIFFERENT PROTON PUMP INHIBITORS

Randomized controlled trials have found no evidence of a difference between different proton pump inhibitors in healing esophagitis.

Benefits

No systematic review was found, but 1 good multicenter, double-blind RCT (225 people) was found.[11] No significant difference was found in the proportion of people healed at 8 weeks by lansoprazole, 30 mg, versus omeprazole, 20 mg, in people with erosive esophagitis (absolute risk healing at 8 weeks: 85% with lansoprazole and 87% with omeprazole; ARR 2%, 95% CI –6% to +14%; relative risk reduction [RRR] 2%, 95% CI –7% to +16%). Relapse rates were not evaluated. Another double-blind RCT (202 people) compared the use of rabeprazole, 20 mg, with that of omeprazole, 20 mg, and found no significant differences in efficacy in healing of erosive and ulcerative esophagitis at 4 weeks (81% for both) and at 8 weeks (92% for rabeprazole *vs* 94% for omeprazole; ARR 2%, 95% CI –3% to +15%).[12]

Harms

No differences in adverse effects were reported, but the data are limited.

OPTION: MEDICAL VS SURGICAL TREATMENT

Medical and surgical treatment have not been adequately compared in RCTs. Preliminary data suggest that proton pump inhibitors and fundoplication are about equally effective at healing. No good comparative data on preventing relapse or complications were found.

Benefits

Healing

One RCT (243 men and 4 women) compared medical versus surgical treatment in people with complicated gastroesophageal reflux disease (erosive esophagitis, Barrett's esophagus, stricture, or esophageal ulcer).[13] It compared continuous medical treatment (antacids, ranitidine, metoclopramide, or sucralfate), medical treatment of symptoms only, or open fundoplication. Evaluation was performed at 6 weeks (201 people), 1 year (176 people), and 2 years (106 people). Those receiving fundoplication had significantly better results, measured by a symptom score (78 vs 88 vs 90), and grade of esophagitis (1.5 vs 1.9 vs 2.2; P <0.03).

Preventing relapse

The trial did not evaluate relapse rates. Uncontrolled trials on the long-term results of open fundoplication found that as much as 90% of people continue to benefit 6 to 20 years after surgery in relief of symptoms, reduced acid exposure on pH monitoring, and absence of inflammation on endoscopy.[14-16]

Preventing complications

No good data relating to this outcome were found.

Harms

The RCT found no operative deaths, but operative complications occurred in 15% and postoperative complications in 18% of people.[13] Uncontrolled studies found that intraoperative complications included splenic trauma (0%-4%), viscus perforation (1%-2%), and less commonly, abscess or inadvertent vagotomy. Immediate postoperative complications included pleural effusion, pulmonary embolism, or late abscess formation. Although morbidity was substantial, mortality related to the surgery was usually less than 1%. Late adverse effects related to fundoplication included bloating, dysphagia, gastric herniation, or breakdown of the fundoplication. Reoperation was required in up to 15% of people for either complications or failure.

Comment

Erosive esophagitis, stricture, and Barrett's esophagus are now known to require at least a proton pump inhibitor for healing and maintenance of remission.[6-8,17] The use of only an H_2 antagonist in the RCT[13] may have biased the results in favor of fundoplication. Preliminary data from 1 RCT suggest approximately equal treatment efficacy when comparing fundoplication with omeprazole for people with erosive esophagitis at 3-year follow-up.[18] Individual patient characteristics may direct the physician toward medical or surgical treatment. Some people are refractory to proton pump inhibitors[19] or have severe "mechanical" reflux requiring surgery. Some people may be high-risk surgical candidates or have relative contraindications to reflux surgery (such as scleroderma, multiple prior laparotomies, or previous gastric surgery). Younger people may prefer surgery to lifelong drug treatment. No studies addressing these issues were found.

OPTION: DIFFERENT SURGICAL TECHNIQUES

No RCTs were found that compared Nissen, Tope, or Dor fundoplication or Hill gastroplasty, nor were RCTs found that compared open versus laparoscopic approaches.

QUESTION: What are the effects of treatment in nonerosive esophagitis?

OPTION: PROTON PUMP INHIBITORS VS H_2 ANTAGONISTS

Proton pump inhibitors have been found in RCTs to be more effective at relieving symptoms than H_2 antagonists, with or without prokinetic agents.

Benefits

Symptom relief

No systematic review was found, but there were 3 good double-blind RCTs. One RCT compared the use of omeprazole, 10 mg, versus cimetidine, 800 mg daily (149 people), and found that after 24 weeks, considerably more people taking omeprazole were free of symptoms (ARs 45% vs 15%; ARR 31%, 95% CI 13%-50%; RRR 205%, 95% CI 85%-334%; number needed to treat: 3, 95% CI 2-8).[20] Another RCT compared the use of omeprazole, 20 mg, versus that of cimetidine, 400 mg (108 people), and found significantly greater symptom relief in those taking omeprazole (66% free of heartburn with omeprazole vs 31% with cimetidine; ARR 34%, 95% CI 21%-46%).[21] Similar results were found when treatment with omeprazole, 20 or 10 mg, was compared with that of cisapride, 40 mg (10 mg 4 times a day).[22] In most trials, symptom relief was about twice as good with omeprazole. Omeprazole has also been found to be superior to ranitidine when measured by symptom scores and scores of psychological well-being.[23,24]

Recurrence

No good data were found on recurrence rates.

OPTION: SURGICAL TREATMENT

No RCTs were found that compared medical with surgical treatment in people with nonerosive esophagitis, and none were found that compared different surgical techniques.

Comment

Good long-term trials are needed that compare laparoscopic fundoplication with proton pump inhibitors, taking into account symptom relief, adherence, prevention of complications, and adverse effects of treatment.

QUESTION: Does treatment of gastroesophageal reflux disease reduce the risk of progression of Barrett's esophagus?

No good evidence was found of the effects of treatment of gastroesophageal reflux in people with Barrett's esophagus.

Benefits

No RCTs were found. Uncontrolled studies that looked at the long-term effect of either cimetidine, ranitidine, or fundoplication in people with Barrett's esophagus found no significant effect.[25,26] One uncontrolled study of proton pump inhibitors found evidence of regression of Barrett's esophagus,[27] but other uncontrolled studies found no evidence of regression.[28,29] None of these studies observed more than 27 people. Small long-term studies of the effects of fundoplication on Barrett's esophagus found that effective fundoplication (defined by ambulatory pH monitoring, symptoms, and endoscopy) may lead to regression.[30,31]

Harms

Weak evidence was found of the harms of treatment of gastroesophageal reflux in people with Barrett's esophagus. Small long-term studies of fundoplication suggest that after failed procedures, there may be progression to dysplasia and carcinoma.[30,31]

Comment

Few centers see enough people with Barrett's esophagus to perform long-term RCTs. In addition, our poor under-

standing of the pathophysiologic characteristics of Barrett's esophagus means that what end point of treatment of gastroesophageal reflux—symptom relief, healing, elimination of acid reflux— that may change the course of Barrett's metaplasia is not known. Whether progression can be measured endoscopically is also not clear.[32,33] Only a long-term, multicenter trial will be able to answer these questions.

QUESTION: Does the treatment of gastroesophageal reflux alter outcome in people with extraesophageal manifestations of gastroesophageal reflux disease?

Limited and conflicting evidence was found from RCTs in people with asthma and symptoms of reflux. No RCTs were found that looked at the effects of treatment on other extraesophageal manifestations (see table).

Asthma

One RCT (double-blind, placebo-controlled crossover design, 25 people with adult-onset asthma and symptoms of reflux) compared treatment with omeprazole, 40 mg per day, with that of placebo.[34] The design included a washout and a crossover period. Symptoms and results of pulmonary function tests were monitored. Omeprazole improved evening peak expiratory flow rates and lessened reflux symptoms, but there was no significant difference in asthmatic symptoms or treatment requirements or in lung function (forced expiratory volume in 1 second, forced vital capacity, histamine bronchial responsiveness, and daytime peak expiratory flow rate), although the confidence intervals were wide. One prospective open-label cohort study evaluated the use of omeprazole in people with nonallergic asthma and reflux symptoms.[35] The mean asthma score improved in people receiving omeprazole but not as significantly as pulmonary function study results. Abnormal proximal acid exposure on pH monitoring and a history of frequent regurgitation were good predictors of clinical response.

Two RCTs compared the use of H_2 antagonists with placebo (1 included a surgical treatment arm). The first was a double-blind crossover RCT of ranitidine, 150 mg twice a day, versus placebo in 48 people with asthma with abnormal findings on pH monitoring.[36] It found no significant improvement in bronchial reactivity, lung function, or peak flow. The second (90 people with adult-onset asthma and reflux) compared placebo, cimetidine, and fundoplication. It found significant improvement in the results of pulmonary function tests and the need for asthmatic medication with active treatment (surgery moreso than cimetidine), whereas the placebo group worsened.[37] Both active treatments achieved long-term benefit (nearly 6 years), the greatest being in the surgically treated group (after a mean of 77 months, 11 of 22 [50%] receiving surgery still had respiratory symptoms vs 19 of 20 [95%] receiving placebo; ARR 45%, 95% CI 5%-85%; NNT 2, 95% CI 1-19). One RCT (247 people with gastroesophageal reflux disease but without obvious lung disease) found no improvement in pulmonary function after 1 year of either medical treatment or fundoplication.[38]

Other extraesophageal manifestations

No RCTs were found. One prospective open-label cohort study of the use of omeprazole in 182 people with chronic laryngitis and reflux found improvement.[39]

Harms

No good data were found on the harms of treatment of gastroesophageal reflux specifically in people with extraesophageal symptoms.

Comment

The link between extraesophageal symptoms and gastroesophageal reflux is by association; symptoms are multifactorial, making it hard to prove that gastroesophageal reflux is the primary cause. There was little standardization in these trials with regard to treatments used or patient characteristics. Before good RCTs can be performed, further research must first identify clear criteria for reflux as the cause of these syndromes.

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Whatever questions, comments, or other contributions you have, we'd like to receive them. We realize that it's experience like yours that makes the journal come alive. Please send your questions, ideas, or comments to us by email: wjm@ewjm.com.

The glitazones: proceed with caution

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INTRODUCTION

Type 2 diabetes mellitus is characterized by the early onset of insulin resistance. Reduced responsiveness to normal circulating levels of insulin leads to hyperinsulinemia. When the pancreas is unable to keep up with increased insulin requirements, hyperglycemia ensues. This can influence the development of diabetes mellitus, obesity, hypertension, and dyslipidemia.[1-3] Commonly referred to as "syndrome X," these complications are associated with an increased risk of coronary heart disease.

A new class of drugs, the glitazones, offers the first therapeutic option specifically targeting insulin resistance. The drugs act on tissues such as liver and skeletal muscle, sensitizing them to insulin action, and thereby increasing glucose uptake and decreasing its hepatic output.

Summary points

- The glitazones are indicated for the treatment of type 2 diabetes
- Clinical research has unveiled a unique mechanism of action and appreciable efficacy for these drugs
- Despite promising preclinical data, case reports of liver toxicity, weight gain, and edema have been published
- Troglitazone has been removed from the market by the Food and Drug Administration because of concerns about its safety
- The poor safety record and high costs of glitazones preclude their use as monotherapy
- Glitazone use has a role, in combination with insulin, sulfonylurea, or metformin
- Patient benefits can be achieved through careful and appropriate prescribing and monitoring practices

THE GLITAZONES

Troglitazone

The oldest and best studied of the glitazones is troglitazone. Clinical trials in the past have examined its use either as monotherapy or as treatment in combination with metformin, sulfonylureas, or insulin.[4-27] These confirmed its ability to decrease fasting plasma glucose and hemoglobin (Hb) A_{1c} concentrations. The US Food and Drug Administration (FDA), however, withdrew the drug from the market on March 21, 2000, because of concerns about its safety.

Rosiglitazone

Nine clinical trials of rosiglitazone have been carried out.[28-36] Average decreases in Hb A_{1c} concentrations ranged from 0.3% to 1.6%. Two of the clinical trials looked solely at fasting plasma glucose levels, reporting decreases from 15.8 to 45.9 mg/dL (0.9 to 2.6 mmol/L).[33,36]

Monotherapy trials comparing once-daily dosing with twice-daily schedules reported enhanced efficacy with the latter. Optimum dosing schedules have not been studied in combination treatments.

In one study of patients taking insulin, there was a 4.8% to 9.4% decrease in daily insulin requirements when rosiglitazone was added.[35] However, symptoms of hypoglycemia were observed more frequently in patients receiving this combination than in patients receiving insulin alone.[35]

Another study compared the safety of rosiglitazone when used in patients older and younger than 65.[28] Most adverse effects were classified subjectively as mild or moderate, with a similar incidence of each in patients from both age groups. Notably, edema was reported in 3.0% to 4.8% of patients on either single-agent or combination therapy.

Pioglitazone

Six trials studying the efficacy of pioglitazone for use in diabetes have been published in abstract form.[37-42] According to the product labeling, pioglitazone decreases Hb A_{1c} levels compared with placebo by an average of 1.0% to 1.6% when used as monotherapy and 0.7% to 1.3% when used in combination regimens. Although the manufacturer promotes pioglitazone as having a positive effect on serum lipid profiles, clinicians should be aware that at least some of the patients studied were simultaneously taking β-hydroxy-β-methylglutaryl-CoA reductase inhibitors. Thus, it is not possible to comment on the true effects of pioglitazone on serum lipids.

EFFICACY AND SAFETY

Despite subtle differences between rosiglitazone and pioglitazone, a review of the literature reveals that they differ little in efficacy. Analysis of the pooled trial data shows that the 2 agents still on the market are more effective than placebo in reducing fasting plasma glucose and Hb A_{1c} concentrations, and the response rates are correlated with daily dosages.

Prevailing clinical wisdom suggests that glitazone therapy should be initiated with full therapeutic doses and that therapy should be discontinued if no clinical improvement occurs within 8 to 12 weeks. The need for prompt discontinuation in patients receiving marginal or no benefit is driven by evidence of 3 serious toxic effects associated with these agents: hepatotoxicity, edema, and

Table 1 *Comparison of FDA-approved indications and dosing recommendations for the 2 approved glitazones*

Drug	Rosiglitazone	Pioglitazone
HMC/UWMC drug formulary status	Formulary	Nonformulary
Date of FDA approval	5/25/99	7/15/99
FDA-approved indications	Monotherapy; combination with metformin	Monotherapy; combination with insulin; combination with sulfonylurea; combination with metformin
Tablet sizes, mg	2, 4, 8	15, 30, 45
Manufacturer recommended dose	Combination: 2 mg bid, 4 mg daily to bid, 8 mg daily	Combination: 15-30 mg daily
Contraindication	ALT > 2.5 × ULN	ALT > 2.5 × ULN
ALT monitoring frequency	ALT at baseline, every 2 mo for 1 yr, then periodically	ALT at baseline, every 2 mo for 1 yr, then periodically

FDA = Food and Drug Administration; HMC = Harborview Medical Center/Unversity of Washington Medical Center; bid = twice daily; ALT = alanine aminotransferase; ULN = upper limit of normal.

weight gain. Evolving reports of these adverse effects have led to a sharp decline in glitazone use.

Hepatotoxicity

At least 43 cases of acute hepatic failure have been reported in patients taking troglitazone after the FDA initially approved its use in 1997. Of these, 28 deaths occurred.[43-49]

The association between liver toxicity and the 2 other glitazones is less clear. Analysis of 3,455 patients treated with rosiglitazone in double-blind, placebo- or active-controlled trials showed no evidence of hepatotoxicity.[50] However, 2 cases of hepatotoxicity following rosiglitazone use have been reported.[51,52] At this time, no reports of liver damage linked to pioglitazone have been published. Strict adherence to guidelines for monitoring liver aminotransferase levels in patients treated with glitazones is the cornerstone of their safe prescribing (table 1).

Edema and weight gain

In addition to sporadic reports of hepatotoxicity, other phenomena such as fluid retention, blood plasma volume expansion, and edema appear to be a glitazone class effect. According to current manufacturer recommendations, the drugs are not indicated for patients with New York Heart Association class 3 or 4 status, unless the benefits of therapy are expected to outweigh the risks. Two cases of troglitazone-induced edema have been reported.[53] One patient developed lower extremity edema after 8 months of therapy. Troglitazone was discontinued, and the patient subsequently lost 7.1 kg (16 lb) within 3 weeks. The second patient presented with orthopnea and edema at 9 months, and following drug discontinuation 12 months later, lost 9.1 kg (20 lb) over 3 weeks.

Clinical observations at the University of Washington/Harborview Medical Center, Seattle, suggest that patients with preexisting edema may experience symptom exacerbation on initiation of glitazone therapy. It is important for physicians to monitor these patients and to record body weights frequently as a means of detecting possible fluid overload and the onset or worsening of edema.

Trials report significant weight gain for patients receiving glitazones.[22,27,29,31-33,35] The experience of our Diabetes Care Center, summarized in 2 case reports,[54] indicates that the weight gain from glitazones is greater than that suggested in the product literature. In these 2 patients, fluid retention was a large and substantial component of the weight gain. After fluid status normalized, however, both patients remained above their starting weights 7 and 12 months after troglitazone discontinuation. These drugs may, therefore, cause weight gain through other mechanisms, perhaps involving the stimulation of fat accumulation.[55-57]

SHOULD GLITAZONES BE USED IN MONOTHERAPY?

Rosiglitazone and pioglitazone are approved for use as monotherapy. But their single-agent use is precluded by concerns about safety, the high drug costs (table 2), and the costs of mandatory liver function monitoring. Until these issues are addressed, insulin, metformin, and sulfonylureas remain less expensive and safer alternatives.

Table 2 *Monthly University of Washington Medical Center/Harborview Medical Center outpatient charge for rosiglitazone**

Drug strength and dosing schedule	Patient charge, $
2 mg orally twice daily	71.06
4 mg orally daily	49.01
4 mg orally twice daily	98.03
8 mg orally daily	89.45

*As of May 24, 2000.

CONCLUSION

Despite advances in pharmacotherapy, type 2 diabetes continues to be underdiagnosed and undertreated. By selectively unlocking insulin resistance, glitazones can be used for carefully selected patients to achieve better glycemic control. When properly prescribed and carefully monitored, they can effectively reduce fasting plasma glucose and Hb A_{1c} levels in some patients.

Continued reports of serious adverse effects, however, hinder their widespread use and acceptance. To receive maximum benefit from these drugs, patients require repeated body weight measurements, periodic liver function tests, monitoring of plasma glucose and Hb A_{1c} concentrations, and adherence to follow-up appointments and lifestyle modifications. The unknown potential for long-term morbidity, the relatively high cost of therapy, and reports of hepatotoxicity, edema, and weight gain all argue against monotherapy. Rather, these insulin sensitizers are more appropriately considered complementary to other oral antidiabetic drugs.

This article was previously published in an expanded form in *Drug Therapy Topics,* a monthly publication from the University of Washington/Harborview Medical Center Drug Information Center. Full text is available on the World Wide Web at http://depts.washington.edu/druginfo.

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Netphiles

We welcome suggestions for Web sites to be included in future Netphiles

Exploring the genome

Progress is being rapidly made on the human genome project. It is the power of information processing technology that has made such achievements even thinkable; and that power is also used to allow instantaneous communication of results to a global network of collaborating (and competing) researchers. The starting point for exploring their work is http://www.ncbi.nlm.nih.gov/genome/seq/.

Just contemplating the volume of data that the site has to serve now takes your breath away; when the sequence is complete it will be truly awesome. With such demands it is fitting that the site's design clothes its content in a user interface of beguiling simplicity. On a web choked with gratuitous graphics, this site uses them entirely appropriately. The site is organized by chromosome. Each is linked to a page that describes the current progress with mapping its genes and shows a more detailed graphic of the chromosome. Areas already sequenced are marked with red and orange bands. Click on a band and up come the genes themselves, represented as vertical blue lines. Pick a line, and the gene sequence itself, in all its ggcgtgaatt gloty, downloads to your browser. (Tourists should not do this too often: 200 kilobases generates a bandwidth-choking file of more than 200 kilobytes: so look for a short one). If you have a gene sequence to identify, the site's BLAST feature (http://www.ncbi.nlm.nih.gov:80/BLAST/) enables the search to be made in reverse. A comprehensive review of this site's informational features requires a PhD in molecular genetics. Those of us not so endowed might begin with a glossary (http://www.ornl.gov/hgmis/publicat/glossary.html) and a primer in human genetics (http://www.bis.med.jhmi.edu/Dan/DOE/intro.html).

Douglas Carnall, *BMJ*

Curbside Consult

Do high factor sunscreens offer protection from melanoma?

Sunscreens were primarily designed to prevent sunburn.[1] Epidemiologic studies have shown that people with a history of sunburn are at greater risk of developing cutaneous melanoma. Because sunscreen use delays the occurrence of sunburn, and also delays the onset of a variety of other ultraviolet-induced skin lesions,[2] these products have been advocated for the prevention of skin cancer. It is generally assumed that the greater the ability of a sunscreen to delay sunburn, denoted by its sun protection factor (SPF), the greater its protection against melanoma.

High SPF suncreen does not protect against sunburn during intentional sun exposure

The laboratory data on the properties of sunscreen have been challenged by results of epidemiologic studies. These findings showed that sunscreen use was associated with an increased, not a decreased, risk of cutaneous melanoma.[3,4] Results of recent studies of sunscreens have failed to show any link between the SPF and the prevention of skin nevi.[5]

Jennifer S Altman/AP

If he's wearing high SPF sunscreen, he may be increasing his risk of melanoma

Epidemiologic data suggest that behavioral issues could be involved in this association between high-factor sunscreen and melanoma. In one double-blind, randomized trial, people who used higher SPF sunscreens during intentional sun exposure, such as sunbathing, were exposed to the sun for a longer period of time.[6] The ability of sunscreen to delay sunburn occurrence probably encouraged people toward longer exposure. Increasing the quantity of sunscreen applied to the skin may also have this effect on people's behavior.

Sunscreen use was associated with an increased, not a decreased, risk of cutaneous melanoma

If the use of high SPF sunscreen leads people to stay longer in the sun, and possibly increases the risk of melanoma, is it still wise to use a sunscreen?

In situations of nonintentional sun exposure, which occurs during daily life, the answer is "yes." Skin areas usually exposed in this way are the head and neck, the hands, and the forearms. Such exposure occurs during outdoor activities such as gardening and skiing. The trunk is rarely involved.

Several randomized trials have shown that the use of high SPF sunscreen during nonintentional exposure reduces the occurrence of actinic keratosis and squamous cell carcinoma.[7,8] Regular sunscreen use during such exposure also reduces the risk of sunburn.[9] It is therefore possible that sunscreen use during nonintentional exposure may reduce the risk of melanoma, although this hypothesis remains unproven. As discussed, the use of high SPF sunscreen does not protect against sunburn during intentional sun exposure.[6,10] It therefore seems unlikely to offer protection against melanoma in this situation.

So how should we advise people? In everyday outdoor life, sunscreen is a useful part of a global strategy of sun protection. This strategy includes staying clothed and covered and taking steps to reduce time spent in the sun. Sun seekers who insist on indulging in intentional sun exposure should be warned that sunscreen use could involuntarily increase their exposure, especially if they use a high SPF sunscreen product.

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Can bleeding problems present initially during sports activity?

Bleeding problems rarely present as a result of sporting injury. They are either congenital or acquired, and most congenital problems present in early childhood, when toddlers begin to walk and fall over.

There are, however, some disorders that are milder and may result in hematoma formation as a result of sports contact or injury; von Willebrand's disease is the most common. Also, some hereditary disorders involving platelets may manifest by easy bruising; patients with these disorders may require referral to a specialist for diagnostic assessment. Most cases of easy bruising are not associated with any hematologic abnormality. A bleeding time is a useful means of assessing the status of such patients, but a detailed history, including family history, and a clinical examination are prerequisite and are best undertaken by a specialist.

Aspirin and other nonsteroidal anti-inflammatory drugs can lead to easy bruising in healthy people. Thrombocytopenia is a fairly common, usually transient condition that is associated with easy bruising and infectious mononucleosis. Splenic rupture can occur when a player who is convalescing from infectious mononucleosis participates in a contact sport, such as rugby. Other coagulation problems, fortunately, are rare and usually are associated with such severe illnesses that the patient is not fit to participate in recreational or competitive sports.

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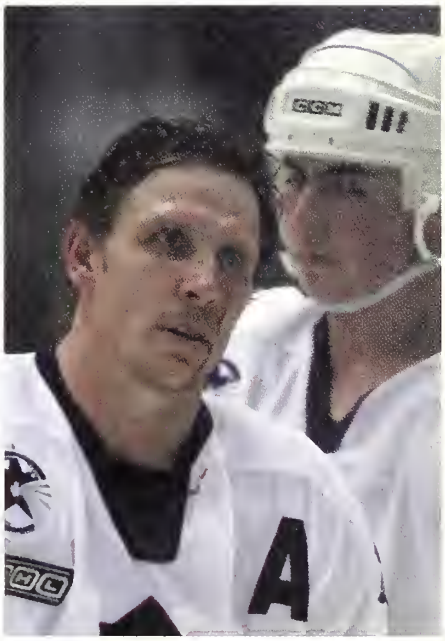
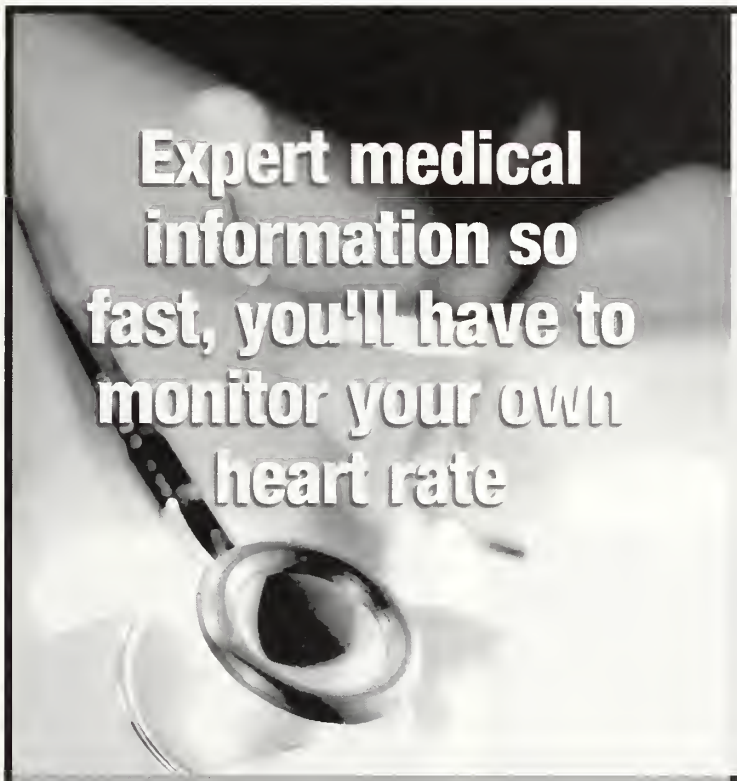


Frank Gunn/AP

Bleeding disorders rarely present as a result of sports injuries



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Chronic lower limb ischemia

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Peripheral vascular disease commonly affects the arteries supplying the leg and is mostly caused by atherosclerosis. Restriction of blood flow due to arterial stenosis or occlusion often leads patients to complain of muscle pain on walking (intermittent claudication). Any further reduction in blood flow causes ischemic pain at rest, which affects the foot. Ulceration and gangrene may then supervene and can result in loss of the limb if not treated. The Fontaine score is useful when classifying the severity of ischemia (see box).

Although many patients with claudication remain stable, about 150 to 200 per million of the population progress to critical limb ischemia (Fontaine III or IV) each year. Many patients with critical limb ischemia can undergo revascularization, which has a reasonable chance of saving the limb. A recent audit by the Vascular Surgical Society found a success rate of over 70% for these patients. Many patients, however, still require major amputation. Rehabilitation of elderly patients after amputation can prove difficult and costly.

INTERMITTENT CLAUDICATION

History and examination

A history of muscular, cramplike pain on walking that is rapidly relieved by resting, together with absent pulses, strongly supports the diagnosis of intermittent claudication. Disease of the superficial femoral artery in the thigh (figure 1) results in absent popliteal and foot pulses and often causes calf claudication.

Fontaine classification of chronic leg ischemia

Stage I	Asymptomatic
Stage II	Intermittent claudication
Stage III	Ischemic rest pain
Stage IV	Ulceration or gangrene, or both

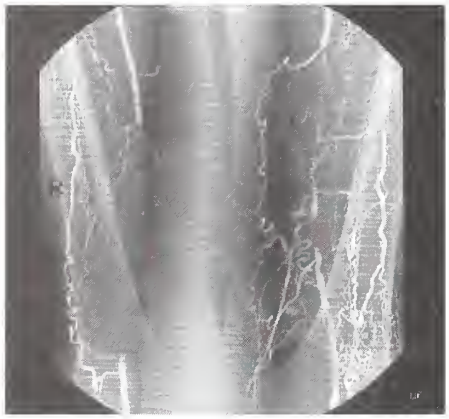

Figure 1 Angiogram showing bilateral occlusions of superficial femoral arteries in thighs. Collaterals arising from the profunda femoris artery can functionally bypass this occlusion.

Disease of the aorta or iliac artery results in a weak or absent femoral pulse, often associated with a femoral bruit (figure 2). Disease at this level may cause calf, thigh, or buttock claudication.

The dorsalis pedis artery lies superficially on the dorsum of the foot, although its position varies considerably (figure 3). The posterior tibial artery lies deeper behind the medial malleolus. Many healthy people have only one foot pulse. The popliteal pulse can be difficult to palpate in muscular patients (figure 4). A prominent popliteal pulse suggests the possibility of a popliteal aneurysm.

Figure 2 Method of palpating the femoral pulse in the skin crease of groin. Counterpressure on the lower abdomen pushes the skin crease toward the inguinal ligament and reduces the risk of missing the pulse.

Differential diagnosis

The pain of nerve root compression can be mistaken for vascular claudication. A careful history can usually distinguish nerve root compression, especially sciatica due to compression of the lumbosacral root. Compression of the cauda equina due to spinal stenosis, however, can be more difficult to diagnose. This condition usually causes pain that radiates down both legs. Although the pain is made worse by walking, it also comes on after prolonged standing and is not rapidly relieved by rest, unlike vascular claudication.

Investigation

Many causes of leg pain can occur in the presence of asymptomatic peripheral vascular disease. Therefore, the absence of pulses does not necessarily imply a causal link. Furthermore, the presence of pulses at rest does not exclude symptomatic peripheral vascular dis-

Figure 3 Method of palpating doralis pedis (A) and posterior tibial (B) pulses. Examine pulses from the foot of the bed, keeping the fingers flat for the dorsalis pedis and using the fingertips for the posterior tibial while applying counterpressure with the thumb.

Figure 4 Method of palpating popliteal artery with patient's knee slightly flexed. Use thumbs to apply counterpressure while palpating the artery, which lies deep in the popliteal fossa, with fingers.

ease. A good history together with an ankle brachial systolic pressure index of less than 0.9 confirms the diagnosis (figure 5).

Exercise testing provides an objective measurement of walking distance and highlights other exercise limiting conditions, such as arthritis and breathlessness. Exercise testing takes time, however, and many patients find it difficult or impossible to walk on a treadmill. Only those with a good history of claudication and normal resting ankle brachial systolic pressure indices require an exercise test.

Duplex ultrasound scanning is useful for delineating the anatomic site of disease in the lower limb (figure 6). Many hospitals still use arteriography for this purpose or when the results of duplex scanning are equivocal. This invasive and expensive investigation should not be requested unless there is a plan to proceed with revascularization, if possible.

Principles of treatment

Intermittent claudication seems a relatively benign condition, although severe claudication may preclude patients from manual work (see box). The risk of generalized vascular disease is probably more important. Patients with claudication have three times higher risk of death compared with age matched controls. Modification of risk factors is therefore vital to reduce death from myocardial infarction and stroke. All patients should be advised to stop smoking and participate in regular exercise. They should also be screened for hyperlipidemia and diabetes. Patients with peripheral vascular disease benefit from regular podiatric care, and those with diabetes should be seen in a foot clinic. Obesity reduces exercise capacity, and losing weight will improve the walking distance.

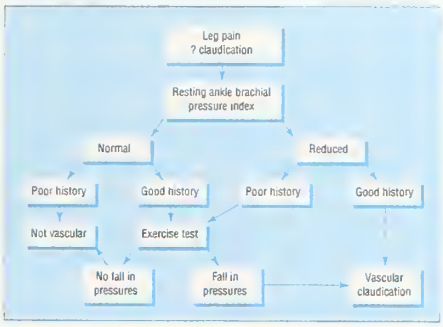

Figure 5 Algorithm for investigation of suspected intermittent claudication

Figure 6 Algorithm for treatment of intermittent claudication

Drug treatment

All patients with peripheral vascular disease benefit from taking aspirin (75 to 300 mg/day) because this reduces the risk of cardiovascular events. Patients who are intolerant of aspirin should take dipyridamole (200 mg twice daily) or clopidrogrel bisulfate (75 mg/day). Naftidrofuryl, currently available in the United Kingdom, may improve the walking distance of patients with moderate claudication (<500 m [<550 yd]), but evidence to support its use is controversial, and its effect on the outcome of the disease is not known.

Exercise programs

A recent meta-analysis of 21 supervised exercise programs showed that training for at least 6 months, by walking to near-maximum pain tolerance, significantly improved painfree and maximum walking distances (figure 7). The only controlled trial comparing an exercise program with percutaneous transluminal angioplasty found that exercise was better. Exercise programs are cheaper than percutaneous transluminal angioplasty or surgery, although long-term compliance seems poor.

Factors that may influence the decision to treat claudication

For	Against
Severe symptoms	Short history
Job affected	Continued smoking
No better after exercise training	Severe angina or chronic obstructive airway disease
Stenosis or short occlusion	Long occlusion
Proximal disease	Distal disease
Unilateral disease	Multilevel disease

Endovascular techniques

The number of percutaneous transluminal angioplasties performed for claudication has risen steeply in recent years. In some situations, endovascular techniques have virtually replaced conventional surgery. Percutaneous transluminal angioplasty seems best suited for stenoses or short occlusions of the iliac and superficial femoral vessels, with 1-year patency rates of 90% and 80%, respectively

Figure 7 Treadmills can be used for objective measurement of walking distance and for exercise training

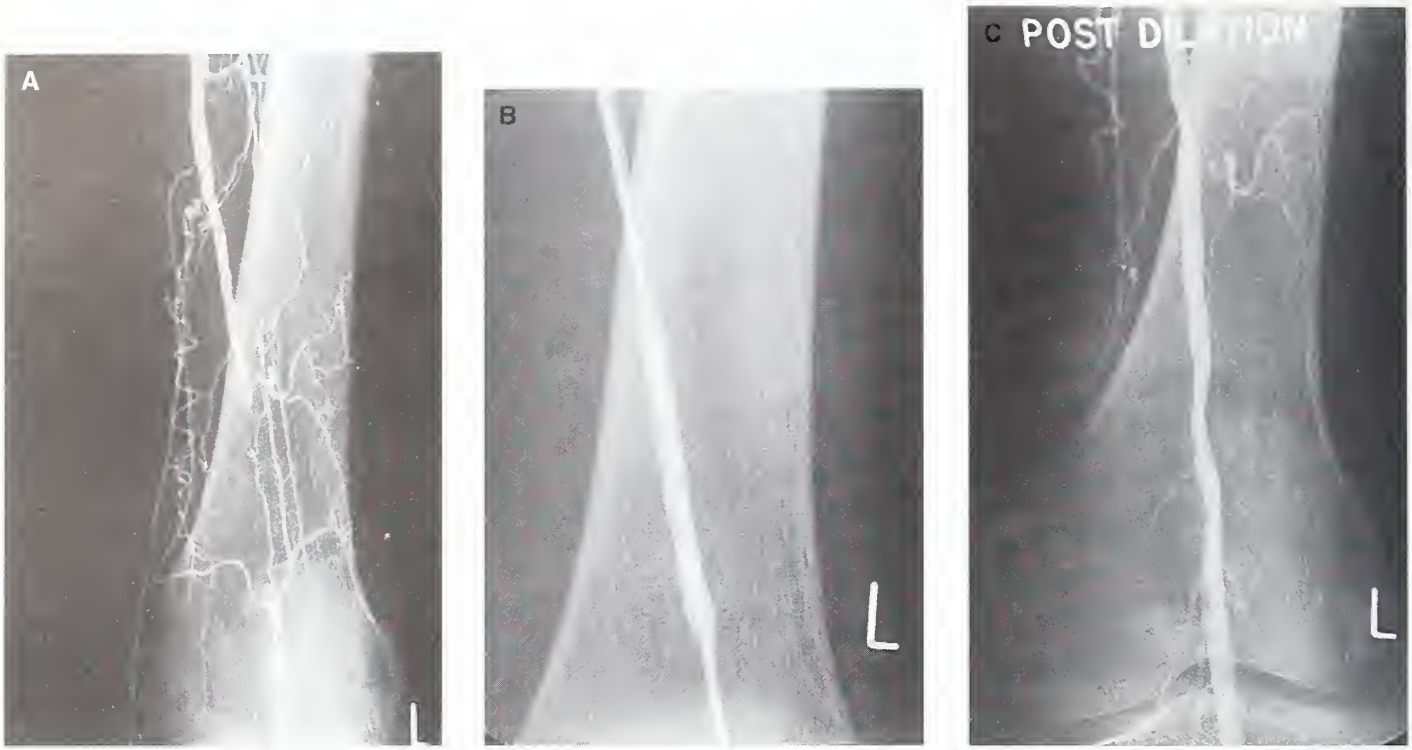

Figure 8 Short occlusion of left popliteal artery (A), treated by percutaneous transluminal angioplasty. The balloon catheter is passed through the occlusion over a guidewire and inflated (B). Appearance after angioplasty is shown in C.

(figure 8). Angioplasty carries a small but definite risk of losing the limb because of thrombosis or embolization, and patients should be informed of this risk.

Metallic stents push back the atheroma and improve on the initial lumen gain after angioplasty alone (figure 9). The indications for iliac stents include a residual stenosis or dissection after angioplasty and long occlusions, but there seems little evidence to justify their routine use. Deployment of stents more distally has produced disappointing results due to high restenosis rates.

Surgery

The role of surgical bypass grafting for longer arterial occlusions remains poorly defined because of a lack of proper trials comparing it with percutaneous transluminal angioplasty and conservative treatment. Polyester (Dacron) aortobifemoral bypass grafts have 5-year patency rates of over 90% but are associated with a mortality of up to 5%. Complications include graft infection and postoperative impotence. Femoropopliteal bypass grafting, using autologous long saphenous vein, polyester, or polytetrafluoroethylene (Gore-Tex) yields patency rates of less than 70% at 5 years. The early patency of prosthetic grafts seems similar to that of vein grafts, although the long-term results seem less good. Femoropopliteal bypass grafts should rarely be used for patients with claudication.

CRITICAL LIMB ISCHEMIA

History and examination

Patients with critical limb ischemia often describe a history of deteriorating claudication, progressing to nocturnal rest pain. Ulceration or gangrene commonly results from minor trauma. Nocturnal rest pain often occurs just after the patient has fallen asleep, when the systemic blood pressure falls, further reducing perfusion to the foot. Hanging the foot out of bed increases perfusion and produces the typical dusky red hue due to loss of capillary tone (figure 10). Elevation causes pallor and venous guttering. Inspect the foot carefully for ulceration under the heel and between the toes. Swelling suggests deep infection. If you can palpate foot pulses, consider an alternative cause of pain, such as gout. Patients with critical limb ischemia require urgent referral to a vascular surgeon.

Investigation

The ankle brachial systolic pressure index is usually less than 0.5. Arterial calcification may result in falsely increased pressures, and caution is needed when relying on Doppler pressures alone, especially in patients with diabetes. All patients with critical limb ischemia should ideally have arteriography with a view to endovascular treatment, if feasible. Duplex scanning may be used instead of angiography and for mapping of the long saphenous vein before distal bypass surgery.

Figure 9 Occlusion of the right common iliac artery before (left) and after (right) insertion of stent

Figure 10 Critically ischemic foot displaying typical dusky red hue on dependency (ischemic rubor)

Dependent Doppler or pulse-generated runoff can help to determine the most suitable artery to receive a distal bypass graft if these cannot be identified by angiography.

Principles of treatment

The same principles and techniques used to treat claudication also apply to critical limb ischemia. Critical limb ischemia, however, is usually caused by multilevel disease involvement, which means that success rates are lower. Treatment focuses on saving the limb (figure 11), although modification of risk factors remains important.

Endovascular treatment

Percutaneous transluminal angioplasty or stenting of proximal disease involvement may relieve ischemic rest pain, but healing of ulceration or gangrene usually requires restoration of foot pulses. This may necessitate extensive angioplasty of the superficial femoral, popliteal, and tibial arteries. Good results have been reported using subintimal angioplasty. Endovascular treatment can also reduce the magnitude of subsequent surgery.

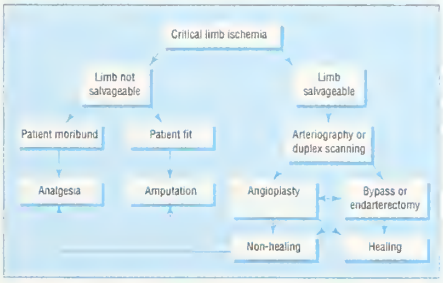

Figure 11 Algorithm for treatment of critical limb ischemia

Surgery

Patients with a pattern of arterial disease considered unsuitable for endovascular treatment will usually require surgery (figure 12). Fit patients with proximal disease involvement benefit greatly from aortobifemoral bypass grafting. In unfit patients, the options include cross-femoral bypass for unilateral disease or axillobifemoral bypass for bilateral disease. These extra-anatomic procedures have lower patency rates. Many patients with distal disease will require bypass grafting to the popliteal or crural arteries below the knee. Autologous vein grafts give the best patency rates (70% at 1 year). Postoperative duplex surveillance may improve patency by permitting the detection and treatment of vein graft stenoses before occlusion occurs.

Amputation

Patients with unreconstructable peripheral vascular disease, fixed flexion deformities, or extensive tissue loss usually require a major amputation. Preservation of the knee joint has enormous advantages for wearing artificial limbs and subsequent mobility. There is little point in risking a nonhealing, below-the-knee amputation, however, if the patient seems unlikely to walk again. Similarly, a patient with good prospects of wearing an artificial limb will fare better with an above-the-knee amputation, if below-the-knee amputation seems unachievable. Local amputation of ulcerated or gangrenous toes will not heal without revascularization.

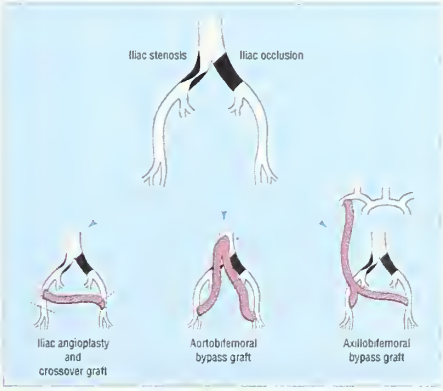

Figure 12 Surgical treatment options for aortoiliac disease

Methods of pain relief for critical limb ischemia

- Slow-release opiate analgesia—for example, morphine sulfate
- Prostacyclin analogues—for example, iloprost or prostaglandin E_1 (alprostadil)
- Chemical or surgical lumbar sympathectomy
- Dorsal column spinal stimulation

Pain relief

Critical limb ischemia causes severe pain that requires narcotic analgesia to provide relief (see box). A slow-release opiate such as morphine seems a good option. Opiates can be supplemented by nonsteroidal anti-inflammatory drugs if these are not contraindicated. Apart from rehydration, adequate analgesia alone may be the best treatment for patients with dementia or other severe comorbidity. If opiate analgesia remains inadequate, then lumbar sympathectomy (surgical or chemical) or spinal cord stimulation may help.

About 20% to 30% of patients with critical limb ischemia have unreconstructable disease. A meta-analysis of 6 randomized trials of a stable prostacyclin analogue found that infusion of this drug reduced the death and amputation rate. Phantom limb pain may complicate major amputation. Amitriptyline hydrochloride, carbamazepine, transcutaneous nerve stimulation, and acupuncture can help in this situation.

This article comes from *ABC of Arterial and Venous Disease*, which is edited by Richard Donnelly and Nick J M London, and will be published this year by the BMJ Publishing Group.

Further Reading

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The predicaments of "dangerous safety": living with juvenile diabetes in 20th century America

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Remedies are not useless because they fall short of their full scope. It is better to keep a man on the edge of a precipice, if you cannot pluck him away from it, than to let him fall over. And many diabetic patients are kept in this predicament of dangerous safety.

Lectures on the Principles and Practice of Physic, 1836-1837
Sir Thomas Watson

Among the remarkable medical accomplishments of the past century, insulin's introduction in 1922 appears miraculous. Emaciated youngsters with diabetes mellitus, kept barely alive through "starvation diets," were resurrected within weeks of starting an insulin regimen. The 1923 Nobel prize awarded to Banting and Mcleod expressed only partially the prevailing enthusiasm and gratitude.[1] Yet, as ensuing decades have taught, the legacy of insulin has had a blackened lining. Delayed diabetic sequelae include damage to the eyes, kidneys, and blood vessels, and the daily burden of living with a chronic illness often weighs heavily on patients.[2-4]

This central tension—between exultation over therapeutic success and concern for dreaded complications—underwrites the modern story of diabetes. Indeed, a similar tension of "dangerous safety" exists for many health care technologies, from neonatal intensive care to bone marrow transplantation to the care of human immunodeficiency viral disease. In each instance, patients' perspectives on their condition and health care, adopted early in the course of illness, can over time lead to long-term emotional and ethical predicaments.

To explore this process, I use a historical case study to describe one patient's experiences with both diabetes and the style of care provided by the renowned Joslin Diabetes Clinic in Boston. From the mid-1910s until his death in 1962, Elliott P Joslin, MD, was an international leader in diabetic care; his protégée, Priscilla White, MD (1900-1989), became an expert on children and pregnant women with diabetes (figure 1). Joslin's vision of ideal diabetic management—marked by a strong Protestant work ethic, a zealous attention to detail, and high regard for self-control—permeated his clinic. Although some patients rebuked his vision, others accepted his philosophy and, unwittingly, the predicaments entailed by his outlook on illness and care.

VIRTUOUS VERSUS PROFLIGATE PATIENTHOOD

In the winter of 1940, 15-year-old John Hansen (a pseudonym) began to lose weight and feel poorly. His physician recognized the classic symptoms and, finding glucose in the young man's urine, referred him immediately to Joslin. John was seen the next day in Joslin's office and then sent to Deaconess Hospital in Boston.[5] The week-long hospitalization marked the beginning of John's career as a diabetic, as he learned about his disease and how to adjust his diet and to administer insulin.[6] In addition, his physicians inculcated values that would prove defining throughout John's life.

Two weeks after discharge, John's mother wrote to White that her son's "attitude remains excellent, with a continued desire to follow his diet rigidly. . . . We are not discouraged because we realize that there is much to be thankful for, especially since we have you to guide us in the right direction."[5] White replied graciously, emphasizing that John's combination of attitude, cooperation, and knowledge—cardinal virtues in the mortal and moral struggle with diabetes—would ultimately determine his outcome.

For the next 2 uneventful years, according to White's notes, the results of John's periodic examinations and blood glucose tests were "perfect," and he remained "really in fine condition," even soliciting her counsel on choosing a college. Then, when he was 18 years old, John failed to live up to the Joslin clinic's strict standard. As White stated curtly, John's test result 3 days earlier was "not as good a test as you should have and I don't think you have been trying quite as hard as you should." White instructed him to increase his insulin dose and added, "I shall want to see you in a month and with better tests."[5]

Summary points

- Insulin and other modern therapeutic innovations have changed type 1 diabetes mellitus (formerly juvenile diabetes) from an acutely lethal disease into a chronic and often debilitating condition
- This process of therapeutic change—which has altered many diseases over the past century—generates states of "dangerous safety"
- For some patients, the attitudes adopted early in their illness toward this dangerous safety can lead to emotional and ethical predicaments
- These predicaments frequently involve issues of control, stigma, risk, and responsibility
- As diagnostic and therapeutic technologies advance further, such predicaments may increase, compelling a reevaluation of fundamental attitudes toward illness and death

Figure 1 Drs Joslin (front row, center), White (front row, right), and the Joslin Diabetes Clinic staff

Notably, John soon penned 2 letters that reestablished his credentials as a "good patient." In the first, written in December 1942, he told White that he had recently disclosed his diabetes on a draft questionnaire and that he needed a letter attesting to his diagnosis. A week later, John again wrote that "due to the current food shortages, my Mother has had difficulty in obtaining meat and butter as required on my diet." He asked White to suggest substitute foods. White responded first with a note to the draft board, reassuring John that, with this in hand, "I am sure they will send you home at once." Several days later, she sent instructions on substituting margarine for butter, fish or nuts for meat, and entrusted him to figure the vegetables and fruits exchanges according to rules he had been taught.[5]

A year passed, and John, attending his college of choice, returned to Boston to be examined. "You are doing splendidly," White enthused subsequently. "Take no chances with yourself," she continued, "but keep on as you are doing. I do think it advisable for you to be checked up at least every 3 to 4 months. It does not take very long. You can bring a book with you if you need to wait."[5]

SAFETY VERSUS DISTANT DANGER

In the summer of 1945, John married. Two years later, he informed White of plans to pursue a doctorate in chemistry before broaching some harrowing questions. Noting that he would not complete the doctorate until his late 20s, he wondered whether his "life expectancy is long enough to warrant my spending another 4 years in school [or would it] seem wiser for me to accept a position now, and thus be able to provide my wife with a home and family for a maximum length of time." He also sought advice regarding "my having children. That is, what is the probability of a child of mine being diabetic (there is no record of diabetes in my wife's family)?" Finally, he requested some medical writing on diabetes because his current knowledge was "limited to what I've gained from Dr Joslin's Diabetic Manual." He was particularly keen "to gain a more technical knowledge, especially concerning what parts of my body will be most likely to fail in later life, and the detrimental (if any) effects of prolonged use of insulin."[5]

White retorted that John's "life expectancy is certainly long enough to warrant your spending another 4 years in school." She stated that the life span of a person with diabetes was three-fourths the normal length, "and of course treatment will be improving during the next few years." She also offered reassurance that "there is no probability of diabetes in your children providing your wife's family history is absolutely correct [that is, 'untainted by diabetes']." Finally, she recommended the most recent textbook that Joslin and colleagues had written on diabetes.[5,7]

NORMAL VERSUS ABNORMAL PERSONHOOD

After his first year of graduate school, John worked the summer of 1948 at a manufacturing plant to learn how his research was applied in industry. On arrival, he had a physical examination. "A doctor (of questionable mentality)," he told White, "placed a stethoscope in the center of my chest for fully 3 seconds, and then after checking me for hernia was about to pronounce me a perfect physical specimen until I was naive enough to tell him I was diabetic. Visibly shaken, the doctor made several hurried phone calls while watching me to see when I would fall into coma." John was told that company policy forbid hiring diabetics. After hasty negotiation, he was retained, but instead of working throughout the plant, he "would be confined within the safe walls of the laboratory."[5]

John fumed: he was "not ashamed to be a diabetic, and until now I have never hesitated to admit it. . . . My health is perfect, I feel fine. . . . Yet, because some moron employed by the mill has gone into coma several times, they believe that all diabetics will do likewise." He asked White to send the company physician a letter to clear up his misconceptions and thus "make it possible for capable and intelligent diabetics to secure jobs in the future—jobs that they have no right to be denied." Mentioning a newspaper article that advocated prohibiting diabetic persons from obtaining driver's licenses, he summed up his feelings: "This type of hog-wash makes my blood boil! I see no reason for the thousands of sensible diabetics to be looked upon as 'industrial hazards' merely because of the mistakes of a few, too idiotic to care properly for themselves."[5]

White replied evenhandedly, explaining why such discrimination existed but was no longer appropriate. She enclosed a letter to the company physician, telling him that antibiotic treatment of infection in patients with diabetes was effective, "so that no longer do we fear infection as we did formerly." White further testified that John "is an extremely intelligent and cooperative patient, recog-

nizes his insulin reactions, and I think the hazards from this point of view [are] also very slight."[5]

This exchange of letters bespoke a deep mutual understanding, dating back to John's first hospital stay, of the key principles of diabetic management—knowledge, attitude, and adherence—preached by the Joslin staff and believed by John. Having built his diabetic identity as an intelligent and conscientious patient, John took knowledge to be a talisman, attitude a defensive weapon, and adherence to regimen his protective armor. Yet, for John, like so many others, the final stages of his life were fraught with difficulty.

SUCCESS VERSUS THERAPEUTIC FAILURE

After returning to graduate school, John was healthy for a decade. In 1959, his fortunes changed drastically for the worse. He wrote Joslin "to obtain any possible advice or help from your clinic which may help prevent my becoming blind." He had suffered a "massive hemorrhage" in 1 eye, followed shortly by hemorrhage in the other. He told Joslin that he "would greatly appreciate your advice or comments as to anything I can possibly do to save what sight I have left." Drawing his letter to a close, John added "some personal comments." As a chemical engineering professor, he fully appreciated "the tremendous research problem involved in this blood vessel damage." What shocked John, however, was his "own naïveté about this problem. From the meager statistics I now can find, I should have expected this development." Pointing a recriminating finger, he asserted that "I do not fear the truth, but I do fear ignorance, and therefore I resent very deeply not being informed truthfully." Contemplating "the personal hell I have gone through trying to rationalize my coming blindness," John was "horrified to think of all the others having to face the same problem with no warning. Yet, I hasten to add, I have been grateful for every day of life I have had since first becoming diabetic. I've always regarded each day as a sort of bonus."[5]

Joslin, who for decades had warned about the endangerment of vision by long-standing diabetes,[8] responded to John, "although what I write will not restore your eyesight, I think you will be thankful to learn what is going on." He informed John that the Joslin Diabetes Center had recently "spent over $200,000 on research for a single year" and that the center cared for "90 patients who have been awarded our Quarter Century Victory Medal because their eyes were certified perfect by [an] expert ophthalmologist." The medal (figure 2), established in 1947 and rewarded to patients who remained free of diabetic complications 25 years after diagnosis, was intended by Joslin to symbolize scientific progress. Joslin reiterated his caveat that "what I write does not bring back your eyesight, but it shows we are not idle, and I feel reassured that our patients are living 3 times as long as formerly and the children . . . have lived some 24 years compared with 1 year at the beginning of the century." He ended by offering his advice to John's physicians regarding how best to manage his diabetes and eye disease.[5]

Figure 2 The Quarter Century Victory Medal

Three years later, John sought to save his vision through an experimental operation that removed part of his pituitary gland.[9] Although this dubious surgical intervention was soon discredited, his eyesight afterward seemed to improve. John's overall condition, however, continued to deteriorate, and when he died a few years later, among the factors cited as leading to his death was the diabetes insipidus that the operation had caused.[5]

THE PREDICAMENTS OF DANGEROUS SAFETY

Being mortal, we all live in states of dangerous safety, our lives distinguished by the degree of hazard, our awareness of potential peril, and our attitude toward risk. John's engagement with his illness highlights 4 challenges—involving control, stigma, risk, and responsibility—that arise when living in the shadow of a threat. First, how can a patient live with a danger that eludes full control, and how can a sense of safety be enhanced without lapsing into false reassurances, magical thinking, or judgmental moralizing? Second, how can health care mitigate the stigma that accompanies life-threatening conditions, reducing its detrimental effects on self-concept and preventing social injustice? Third, how can risk assessment be incorporated into a vibrant care plan, allowing patients to move ahead

joyously with life while addressing the threat of future dangers? Finally, how should responsibility for the sequelae of chronic disease be apportioned between patients and physicians, fostering patient empowerment while avoiding antagonism, blame, or inappropriate abdication of professional responsibility?

These predicaments, which occurred throughout John's life, intensified when his eyesight was threatened. For John, the crisis prompted his protest—not fully supported by his medical record—that he had been left uninformed. Nevertheless, he continued to look to his physicians for guidance and hope, striving poignantly in the final sentences of his last letter to strike a balance between outrage and obligation, gratitude and grief. Joslin's response, on the other hand, bespoke his abiding faith: taking the longer view, he accepted the painful misfortunes of 1 patient by focusing on the trend toward better outcomes for many people with diabetes and by working devotedly to improve clinical care for all.

Recounting how this patient and physicians struggled to make sense of a threatening chronic illness at a personal level illuminates our collective struggle with the frustration associated with chronic debilitating conditions. Reacting to this frustration, our culture has typically sought further technical innovation, desiring to remove the root causes of suffering and death. Yet, given advances in diagnostics, we are likely to become more aware of the specific diseases that threaten us. Advances in medical therapy will keep us living longer in states of dangerous safety. Perhaps, then, we pursue a goal that guarantees frustration, as technology shifts but never eradicates the predicaments of our mortality. If so, our fundamental perspective on health needs to change, accommodating the inescapable threats of illness and death into the concept of a well-lived life.[10,11]

This study was approved by the human subjects review committee of the Joslin Diabetes Center, Boston, and all primary historical materials are from their archives. My enduring thanks to Jim and Susan Warram, who pointed me in the right direction and graciously helped with all that followed. I am solely responsible for the facts and views presented in this article.

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Iranian births

A lesson in cross-cultural care

Information about cultural patterns in this article and others in this series represents generalizations, which should not be mistaken for stereotypes. Cultural generalizations will not fit every patient, but awareness of broad patterns can give practitioners a starting point from which to provide appropriate care. The information on Iranian births in this article is taken from H Hafizi's chapter in *Culture and Nursing Care: A Pocket Guide*, edited by J G Lipson, S L Dibble, and P A Minarek.

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The most difficult patient that Susan, a labor and delivery nurse, ever attended was Robabeh, an Iranian woman. Robabeh yelled and screamed throughout her entire uncomplicated labor. After the delivery of their infant, Robabeh's husband gave her a 3-karat diamond ring. When Susan commented on the expensive gift, Robabeh explained dramatically that it was because "He made me suffer so much." It is customary among Iranians to compensate the woman with expensive gifts for the suffering she experiences during childbirth; the greater the suffering, the greater the gifts, especially if the child is a boy. No one will know how much she is suffering if she does it in silence.[1]

PREGNANCY CARE

Prenatal care depends on financial stability.[2] The family provides help and support. An expectant mother is en-

Behrouz Mehri/STR

Iranian women in the holy Shiite city of Quom

couraged to balance diet and rest adequately and to refrain from heavy work throughout pregnancy.

LABOR PRACTICES

A midwife or a physician is acceptable at childbirth. Walking before delivery is encouraged, and Iranian women are generally agreeable to Lamaze classes. Expectant fathers are involved and interested in the birthing experience. During labor, a woman should be offered pain relief. Taking a shower soon after birth is common.

ROLE OF THE LABORING WOMAN DURING BIRTH PROCESS

A woman's role during labor depends on her personality. Some will moan and grunt during labor, and others may get hysterical. Modesty remains a controlling factor.

ROLE OF FATHER AND OTHER FAMILY MEMBERS DURING BIRTH PROCESS

More acculturated Iranian fathers take an active role. Female family members are supportive and present.

METHOD OF DELIVERY

Iranian women have no preference for either vaginal delivery or cesarean section. The health of the mother and baby are defining factors.

BREAST FEEDING

Breast feeding is preferred over bottle feeding. Breast milk is mixed with solid food when the infant is about 4 to 6 months of age. Iranian women avoid using prepackaged baby food, and they generally do not mix breast and bottle feeding unless the mother works outside the home. They may continue to breast-feed as long as 1 year.

BIRTH RECUPERATION

Rest, proper diet, hygiene, and emotional ease are considered essential. Female family members and friends provide support and guidance in the care of a newborn.

PROBLEMS WITH BABY

If a baby is diagnosed with an ailment, the best person to speak with is the father of the child. Health care professionals should always give hope and discuss methods of treatment.

MALE AND FEMALE CIRCUMCISION

Female circumcision is never performed. Male circumcision is done either at the hospital soon after birth or at a later date. Male infants are always circumcised and, in some families, the occasion is marked by a period of festivity.

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Giving credit where credit is due

The photographer who captured the beauty of the Na Pali Coast on the cover of our June issue is Homer Hernandez. Dr Hernandez, whose work appeared on the cover of our January 2000 issue as well, lives and practices medicine in Southern California.

West of the Rockies

Speaker's Corner

A breach of "etiquette"?

My father, a 93-year-old retired physician, lives with us. As a high-functioning individual, he takes care of all his personal needs. For a few weeks, he had observed (rather than complained of) a "little more tiredness and weakness." I initially ignored the symptoms, but when they persisted, I thought I should pay them more attention. Beset with guilt, I arranged for a complete blood count and basic chemistry profile. Perhaps he had a touch of anemia that required correction or some errant electrolytes that needed to be brought into line. At 5 PM on a Friday, the laboratory telephoned me at home with the results. His blood chemistry results were normal, but his hemoglobin concentration was 70 g/L (7.0 g/dL) with a mean corpuscular volume of 85 μm^3. The leukocyte and platelet counts were normal, as was red cell morphology.

Malignant disease with bone marrow involvement was my first diagnostic thought. My greatest concern was what I should do now. Despite knowing that hospitals operate 7 days a week, I felt—as do most physicians—that all days are not created equal. I decided to wait until Monday morning to plan admission. After all, the "patient" would be under close observation.

Clearly the opinion of a consultant was necessary, and I had all weekend to decide whose advice I should seek. In an academic institution, specialists abound, and the decision was not easy. Competence was not the issue because, thanks to today's stringent credentialing requirements, an incompetent physician is difficult to find. After much deliberation, I decided to ask a fairly young (but not too young) physician to see my father when he was admitted. The specialist I chose was not a personal friend, but one who had a good reputation for his skill, common sense, and care of patients.

Came Monday morning, and early in the day, I called the physician's office and left a message indicating the reason for my call and asking him to get back to me as early as possible. My intention was to provide him with what little clinical history I had and to send him copies of the blood test results from 3 days earlier—anything to give a helping hand and make his job easier, I thought.

I waited patiently, but by 3 PM, I had not heard from the physician. I had little doubt that he would have received my message, but I stubbornly decided not to call again. At 4 o'clock when he did call, I sensed a slight irritation in his voice: "I have to leave for the university now," he said, "and I won't have the time to see anyone. I will be away all day tomorrow, and so I'll ask one of my colleagues to see your father."

That was the end of the conversation. I felt disappointed and hurt because, while not unfriendly or discourteous, his tone lacked warmth and concern. The next day, the colleague who I did not know and had never met came to see my father. He did not call or speak to me, but his consultation note was elegant. He had clearly taken his time in formulating his impression and recommendations. I am sorry I never met him, for the next thing I heard was that he had left for a new position in another state.

Papers are written, conferences held, and new journals have been created to help us decide what is right and what is wrong in dealing with our patients. This we refer to as "medical ethics." But what of "medical etiquette"? I do not know if there is an official definition for medical etiquette, but I regard it as the code of behavior between physicians, nurses, and other staff concerned in the care of patients. Not to be forgotten is the conduct that professionals in medicine should show toward students and trainees. There is, of course, much overlap between what we loosely call common courtesy and courtesy as it applies in a professional setting. Most are obvious: returning calls within a reasonable time, communicating with dignity, and so on, but some are not so apparent. Professional courtesy is a term that generally refers

to the adjustment (or waiver) of charges when one physician is indebted to another. But there are other forms of professional courtesy. The courtesy of responding to a request to see a physician or a member of the physician's close family is one of them. I consider it an honor to be asked to see a colleague or a colleague's spouse, parent, or child. It is an honor more than any patient can bestow, for of all the physicians available, that physician has chosen me.

Why was I hurt? Was it just because the consultant of my choice did not respond to my request? Possibly, but probably not. There will be occasions when this is impossible, or nearly so. On such occasions, a genuine apology and an explanation of the circumstances are all that is needed. A little thought (or pretence at one), suggesting a colleague by name and saying how likable and good that person would be, would have been sufficient. Am I being unreasonable? Perhaps in the eyes of some I am. But then, we must develop our own code of conduct. That's what etiquette is all about.

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West J Med 2000;173:69-70

Practice Point

Jacob's Story

The referral slip described a lesion on the side of the tongue that needed evaluation. There had been some localized bleeding and pain. This would be the last patient at the end of a long day filled with surgeries, consultations, follow-ups, and numerous phone calls. The physician was already an hour behind schedule.

Jacob was a bright, energetic, middle-aged man with thick brown hair brushed back in a long wave. Despite his youthful appearance, there were deep lines under his eyes. He was a virtuoso musician known for his intense and often emotional performing style. Jacob had a nervous habit of grinding his teeth, something he had noted since childhood. Examination of the mouth revealed an area of inflammation on the side of the tongue, the apparent site of recurrent injury from the intermittent grinding of teeth with secondary biting of the tongue. Further examination of the palate revealed a deep punctate erosion with scarring, a site of previous injury.

"I see an area in the back of your mouth where you appear to have been injured in the past."

Jacob was quick to respond. "Yes. You noticed that. Let's see how good you are. Tell me what you think that is."

"I served as a surgeon in World War II and saw multiple injuries. I believe it is a bullet wound."

Jacob was visibly impressed. His body relaxed. "Yes. When I was young . . . " He stopped to gather his thoughts. "We lived in a beautiful village in Poland. Three sisters, one brother. All of us were involved in music; playing, singing. It was a Sunday when my village was overrun by the Nazis. I had run to the top of a nearby hill. I was 11 years old at the time. I saw them kill my family. One by one they grabbed them and shot them all, even my grandparents. They all struggled to get away but were held down while the soldiers tortured them and then shot them. One soldier spotted me on the hill and ran after me. I ran with all my strength, but he caught up to me, grabbed me by the throat, and rammed his gun into my mouth. I pulled my head back and cried out to God to save me. The soldier twisted my neck. I felt the cold steel of his pistol in my mouth. He pulled the trigger, and I blacked out. I was left for dead. The bullet had missed its deadly target. Amazingly, I survived. I was alone, without my family. My village and country were destroyed. At first I didn't want to live and even tried suicide one time."

He was sobbing. The emotion of the moment was overwhelming. The physician placed his hand on Jacob's shoulder to comfort him. Spontaneously the physician began to cry and said, "I have seen the horror of friends, fellow soldiers, the camps."

It was a small physician's office in a large metropolitan area where physician and patient cried together for a time. They shared stories, exchanged photographs, talked about lost loved ones, fears and hopes for the future. Jacob never required a biopsy or surgery. Healing came with time and support. Follow-up visits continued for a period of time. In the end, the teeth-grinding stopped and the "lesion" healed. Jacob would continue to play in his unique way—a virtuoso musician with compassion and energy. The music expressed so exquisitely his message of renewal and love.

My father told me about his patient, Jacob, as I was starting medical school. That was 20 years ago, and both physician and patient have since passed on, but their story and memory have been a part of my life and those of my students ever since.

Charles M Farr

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Hunger and thirst

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Internally displaced people walk through a dust storm in Denan, Ethiopa, which has recently been stricken by drought. The refugees go in search of food and water, although their efforts are often in vain.

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This month in wjm

Photoelectric smoke alarms have advantages over ionization alarms

Five thousand people in the United States lose their lives from fires each year, and Alaska has the highest fire fatality rate of any US state. Functioning smoke alarms can reduce the risk of death in residential fires, but people often disconnect these devices because of false or "nuisance" alarms. In a prospective cohort study in Alaska, Fazzini and colleagues found that the rate of false alarms and subsequent disconnection was lower with photoelectric smoke detectors than with ionization alarms. But photoelectric alarms are more expensive, says Istre in a commentary on p 92, so these differences should be confirmed before we promote their use.

Ecstasy use can cause cognitive problems

Over 3 million young people in the United States have tried the recreational drug ecstasy at least once. Should doctors be concerned? In a Curbside Consult on p 129, Kelly reviews the accumulating evidence that ecstasy can cause cognitive, mood, and behavioral changes, which may be irreversible. The challenge now is to educate drug misusers about these risks in a nonjudgmental way.

Exposure to electromagnetic fields is associated with suicide

Suicide is the eighth leading cause of death in the United States, and some suicides may be work-related. On p 94, van Wijngaarden and colleagues report an association between occupational exposure to electromagnetic fields and suicide. The authors suggest that the fields may inhibit melatonin production, which could contribute to depression. In a commentary on p 100, Peek-Asa warns that the association may have been due to confounding factors, such as drug use, mental illness, and family stresses.

How to foster hope in the terminally ill

Physicians often assume that hope and terminal illness are mutually exclusive. This is a fallacy, says Rousseau on p 117, because dying patients can still hope for serenity, inner peace, and freedom from troubling symptoms. He describes a number of interventions that can engender hope and improve the quality of life of dying patients.

African American adolescents are neglected in sexual health screening

In a survey of African American adolescents in a low-income neighborhood of San Francisco, Ellen and colleagues found that only 26.2% of sexually active males and 58.5% of females had been screened for a sexually transmitted disease in the previous year (p 109). In a commentary on p 113, Staggers and colleagues suggest that these low screening rates may be due to the failure of physicians to discuss sexuality. They also believe that race is a major barrier to the delivery of primary care services to minority groups.

Editor's Pick

Does the male menopause exist? On p 76, Gould and Petty argue that there is a syndrome of androgen deficiency in male middle age, which leads to hot flushes, mood changes, and sexual dysfunction. But Jacobs disagrees. He says that there is no convincing evidence that these symptoms are caused by a lack of testosterone (p 78). Korenman's position is somewhere in the middle (p 80). He has adopted the term "manopause" for a set of age-related changes of uncertain causation.

The pharmaceutical industry is of course interested in the debate. A testosterone skin patch is already on the market, and a gel will be available shortly. We are likely to see an aggressive marketing campaign, even though the very existence of the male menopause is contentious.

But the debate is valuable because it alerts us to a crisis amongst men. There is growing recognition by physicians of gender inequalities in health. Men in industrialized nations die on average 5 years earlier than women. They have a higher rate of suicide, of death from coronary artery disease under the age of 65, and of hospital admissions due to stroke.

In attempting to address this crisis, there has been far too much focus on specific diseases, like prostate cancer, and not enough on the educational, social, and emotional factors that cause men to ignore their health and to adopt high risk behaviors. For most illnesses, men are less likely to consult their physicians than women. They are more likely to smoke and drink alcohol and are less likely to eat a healthy diet. They more often put themselves at risk of accidents and sexually transmitted diseases.

We should recognize that the burden of men's poor health falls on those who are already marginalized—men of low socioeconomic status and from ethnic minority groups. We shouldn't let the men's health movement be hijacked by drug companies intent to promote testosterone, or by zealous advocates of prostate cancer screening. Promoting men's health means raising responsible men and redressing social inequalities.

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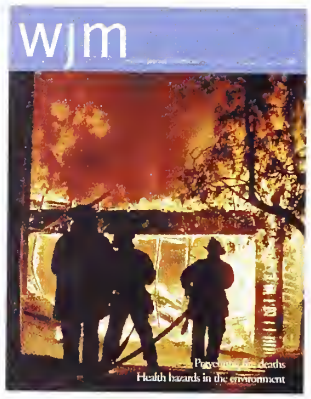

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Op-Ed

The male menopause: does it exist?

FOR: Some men need investigation and testosterone treatment see opposing view p. 78

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The term "male menopause" is inappropriate because it suggests a sudden drop in sex hormones such as occurs in women in the perimenopausal state. It is not an inevitability but may occur mainly in middle-aged and elderly men when testosterone production and plasma concentrations fall. A threshold of plasma concentrations seems to exist, below which symptoms may become apparent. Testosterone concentrations found to be critical for sexual functioning in men lie around 10.4 nmol/L (300 ng/dL), although they vary among individuals.[1] Although some have found that differences in plasma testosterone concentrations within the normal range in young healthy men do not correlate with differences in sexual activity and interest, others have shown that differences in the concentrations of the potent metabolite, dihydrotestosterone, do.[2,3]

Earlier this century, the term "male climacteric" (from the Greek *klimacter*, the rung of a ladder) was used and is more appropriate because it suggests a decline and not a precipitous drop in hormone concentrations.[4,5] A landmark paper of 1944 accurately described symptoms, reversed by testosterone replacement but not by placebo, seen in men suffering from an age-associated decline in testosterone concentrations.[5] Because of the similarity of most of the symptoms between men and women, the term "menopause" gained popularity and has, unfortunately, stuck.

An abnormally low concentration of testosterone (hypotestosteronemia) may occur because of testicular dysfunction (primary hypogonadism) or hypothalamic-pituitary dysfunction (secondary hypogonadism) and may be congenital or acquired.

ENDOCRINOLOGY

In aging men, a reduction in testosterone concentration is due mainly to a decline in Leydig cell mass in the testicles or a dysfunction in hypothalamic-pituitary homeostatic control, or both, leading to abnormally low secretion of luteinizing hormone with resultant low testosterone production. It is well recognized that with normal male aging, mean plasma testosterone concentrations decline, albeit with considerable variability between men and with a broad range in age-related values. Cross-sectional and prospective studies show a decline that starts in early middle age and then progresses in a linear fashion.[6-11] Mirroring this decline in plasma testosterone concentration is an age-associated increase in plasma concentration of sex hormone–binding globulin (SHBG), resulting in a more pronounced decline in the active or bioavailable testosterone moiety.[12-14] Concentrations of bioavailable testosterone decrease by as much as 50% between the ages of 25 and 75 years,[15] and it has been proposed that with respect to bioavailable concentrations, as many as 50% of men older than 50 years are hypotestosteronemic when compared with peak early morning concentrations in young men.[16] With age, a loss of hypothalamopituitary circadian rhythm occurs, which may result in exaggerated falls in plasma testosterone concentrations by evening.

Symptoms of the male climacteric syndrome*
Depression, nervousness
Flushes and sweats
Decreased libido
Erectile dysfunction
Easily fatigued
Poor concentration and memory

*From Heller and Myers[5]

Malcolm Willett

EFFECTS OF HYPOTESTOSTERONEMIA

A quantitative definition of hypotestosteronemia has generally been accepted as 11 nmol/L (320 ng/dL) because only 1% of healthy men aged 20 to 40 years will have a concentration below this limit.[17] The development of hypotestosteronemia may be related to heredity because 60% of the variability of testosterone concentrations and 30% of that of SHBG may be due to genetic factors.[18] A his-

tory of orchitis, testicular trauma, or other pathologic disorder may be contributory. The presence of obesity is associated with lower concentrations of bioavailable testosterone,[19] and insulin concentrations have been found to be indirectly correlated with SHBG and testosterone concentrations.[20] With respect to lifestyle, excess intake of alcohol and physical and psychological stress are all associated with lowered testosterone concentrations.[21,22]

Aging is usually associated with a decline in sexual interest and potency.[23] This suggests that such changes in sexual behavior are androgen-dependent but does not prove the case. Although erectile dysfunction in elderly men is often of nonhormonal cause, testosterone deficiency accounts for 6% to 45% of all cases.[24]

Affective symptoms have long been associated with hypotestosteronemia: depressed mood is significantly correlated with low concentrations of bioavailable testosterone in older men.[14] Some longitudinal uncontrolled studies of hypotestosteronemic men have shown that symptoms of depression, anger, irritability, sadness, and nervousness significantly decreased and friendliness, a sense of well-being, and energy levels improved with androgen treatment.[25,26] Evidence suggests that mood disturbance may be linked to hypotestosteronemia and that testosterone replacement therapy may be beneficial, but placebo-controlled trials are needed to confirm these issues. Fatigue may occur with hypotestosteronemia. During one prospective study, symptoms significantly lessened with supplementation and increased during androgen withdrawal; another showed substantially improved energy levels.[26]

Male aging is associated with an increase in central and upper body fat deposition and reduced muscle mass and strength. This could be explained by an age-associated decline in growth hormone concentrations, which itself is associated with an increase in SHBG and, therefore, a reduction in bioavailable testosterone.[27] The consensus is that testosterone supplementation in hypotestosteronemic men enhances fat-free mass, muscle bulk, and strength.[28,29] Profound hypotestosteronemia in younger men results in accelerated bone loss and osteoporosis.[30] In older men, bioavailable testosterone concentrations are positively correlated with bone mineral density at the radius, spine, and hip,[31] and men with hypotestosteronemia have been reported to be at increased risk of hip fracture.[32] Data on the effects of testosterone replacement therapy on bone metabolism in hypotestosteronemic men are limited but suggest benefit.[33]

Vasomotor disturbance and night sweats occasionally occur, their association with testosterone deficiency and relief by testosterone replacement being noted as far back as the 1930s.[4,5,34] Androgens also have an important role in the development of cognitive functioning, and in men, strong correlations exist between testosterone concentrations and visuospatial abilities in certain domains.[35] Testosterone administration to aging men has been shown to enhance certain visuospatial skills.[36]

Hypogonadism (like hypothyroidism) is a pathologic state and is associated with several other comorbid factors, such as the presence of cardiovascular risk factors (obesity, higher waist:hip ratio; higher concentrations of glucose, insulin, total cholesterol, low-density-lipoprotein cholesterol triglycerides, apolipoprotein B, fibrinogen, and plasminogen activator inhibitor I; and lower concentrations of high-density-lipoprotein cholesterol C and apolipoprotein A-I), which are improved by testosterone administration.[37]

INVESTIGATIONS AND TREATMENT

Whatever the nomenclature, be it male menopause or climacteric or age-related hypotestosteronemia, an investigation should be undertaken for men presenting with symptoms outlined in the box. This should include an assessment of concentrations of plasma gonadotropin, prolactin, and SHBG and early morning concentrations of testosterone. Men with hypotestosteronemia with unequivocal signs and symptoms of androgen deficiency, and when reversible causes of testosterone deficiency and contraindications have been excluded, should be offered treatment with testosterone replacement therapy in line with the current World Health Organization guidelines.[38] This, however, is a specialty beyond the scope of this article.

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The male menopause: does it exist?

AGAINST: Problems of senescence in men are not analogous to female menopause see opposing view p. 76

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The normal menopause—that is, the final cessation of menstruation—is caused by primary ovarian failure. The estrogen deficiency that results often causes vasomotor instability (flushing and sweating attacks), genital atrophy (vaginal dryness and discomfort), and bladder irritability, together with difficulties in cognition and loss of a general feeling of well-being. This climacteric syndrome, readily reversible by estrogen treatment,[1] is obviously gender-specific. We have to ask whether it really provides a helpful analogy for the features Jaques described as the penultimate age of man[2]:

> . . . The sixth age shifts
> Into the lean and slipper'd pantaloon,
> With spectacles on nose and pouch on side,
> His youthful hose well sav'd, a world too wide
> For his shrunk shank; and his big manly voice,
> Turning again toward childish treble, pipes
> And whistles in his sound.

In thinking about this, we do well to consider how many of the changes in men as they pass from middle to old age should be attributed to the passage of years and how many to a decline in hormone concentrations. An endocrine explanation is attractive because it raises the possibility of hormonal therapy for symptoms that occur at this time of life. The findings of a careful review of the literature are at best suggestive. But we still have a way to go.

First, what hormonal changes occur in aging men? Certainly gonadal function wanes: by age 80 years, serum total testosterone concentrations have fallen to about 75% and free testosterone concentrations to about 50% of what they were at age 20.[3] The fall of free testosterone (that is, of the fraction that is biologically available to the tissues) is amplified by a difficult-to-explain but regularly observed increase in concentrations of the sex hormone–binding globulin.[4] The fall in testosterone production is caused partly by testicular failure and partly by changes in pitu-

itary gonadotropin secretion.[4] The key difference from the menopause, however, is the gradual nature of the change in men compared with the precipitate fall of estrogen concentration in women.[5]

Second, what are the biologic changes that can be related to these endocrine alterations? The association of a symptom with a particular hormone concentration does not indicate causation. Therefore, before attributing to testosterone deficiency the reduction in sexual activity, the decline in muscle bulk to which Jaques referred, and the decline in skeletal mineralization that may all occur in elderly men, we are obliged to prove that hormone replacement therapy in physiologic doses reverses these processes. We must, in other words, shift the argument from epidemiologic to interventional studies. The history of this treatment is that it began with a number of persuasive trials of full-dose testosterone treatment of both young and older men with hypogonadism.[6-9] When, however, physiologically appropriate doses of testosterone were administered to elderly men, the results were less impressive. For example, for 3 years, Snyder and colleagues treated a group of almost 100 healthy men older than 65 years with testosterone patches in doses sufficient to raise their serum testosterone concentrations into the range appropriate for men in their 20s.[10] The overall effects on bone mineral density were no different from those obtained with placebo. Although lean body mass increased significantly (1.9 [SD 0.3] kg), principally in the trunk, and fat mass decreased (−2.9 [−>0.5] kg), principally in the arms and legs, Snyder and colleagues were unable to detect a significant increase in muscle strength, as measured in extension and flexion of the knee with a dynamometer.[11]

So far as sexual activity is concerned, the role of testosterone in elderly men is still not well defined.[12,13] Circulating concentrations of testosterone in older men are usually well above those needed for a normal sexual response, although the proportion of men complaining of erectile dysfunction rises dramatically with age, such that 50% of men between the ages of 50 and 70 years complain of impotence.[14] As many as 80% of cases of erectile dysfunction are now thought to have a medical cause, such as diabetes mellitus, cardiovascular disease (especially angina and after myocardial infarction), neurologic disorders (multiple sclerosis and spinal injury), pelvic surgery (prostatectomy), and trauma. Indeed, some have suggested that the development of erectile dysfunction should be regarded as sentinel of disease and an indication for careful medical assessment.

Recent work, reviewed elsewhere,[15] has shown that what ultimately determines potency is the ability of muscles in the walls of the artery supplying the penis to relax and so permit engorgement to occur. Nitric oxide released from parasympathetic nerve endings in response to sexual stimulation causes guanylate cyclase to produce cyclic guanosine monophosphate (cyclic GMP), which relaxes arterial smooth muscle. Cyclic GMP is metabolized by a specific phosphodiesterase. Sildenafil citrate (Viagra) inhibits this enzyme, prolongs arterial relaxation, and so enhances erection. As for impotence in an older man, unless hypogonadism can be clearly shown, treatment with sildenafil (with appropriate warnings about cardiovascular risks and drug interactions with nitrites) is likely to be safer and more efficacious than injections of testosterone esters.

The analogy of the female menopause is not helpful in understanding or trying to manage the problems of senescence in men. Moreover, the endocrinology of aging is much broader than that term suggests. As Lamberts and associates have pointed out, although the fragility of elderly people might be related to a gonadopause, an adrenopause (the age-related fall of dehydroepiandrosterone sulfate concentrations), or a somatopause (the decline in secretion of growth hormone and insulinlike growth factor), actually in old people, the commonest endocrine disorders are diabetes mellitus and hypothyroidism.[16] These conditions are definitely treatable.

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COMMENTARY
"Manopause"

Changes do occur in men with age, and these may be amenable to androgen therapy

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The authors of this debate describe in detail the physiologic changes that occur in men with age. Although we may disagree with the interpretation of the reported findings, the main results are undisputed. With normal aging, which begins before the 4th decade, men have a progressive reduction in testosterone and bioavailable testosterone levels and an increase in SHBG. A relatively meager, if any, gonadotropin response to these sex hormone changes occurs. Levels of dehydroepiandrosterone, growth hormone, and insulinlike growth factor-1 also decline, which is more marked in the later years. Levels of estradiol remain unchanged, as do those of dihydrotestosterone, although blood levels of the latter are a poor reflection of the biologic activity of this predominantly intracellular hormone.

Starting in the late 20s, men undergo a progressive loss of muscle mass and an increase in fat mass, even those who maintain the same weight. Although cognitive function relating to knowledge and memory remains intact until an advanced age, perceptual speed declines steadily from the 4th decade. No convincing evidence indicates that the prevalence of clinical depression increases with age, but, in my experience, subclinical depression in men is both underdiagnosed and under-researched. Sociologic studies of men in developed countries suggest that a feeling of well-being remains constant until the 8th decade.

Beginning about age 50, the prevalence of erectile dysfunction begins to increase exponentially from 5% of the adult male population to more than 50% by age 80 years. Vascular, neurogenic, and psychogenic risk factors play a more important role than hypogonadism in its cause. This is supported by the fact that androgen therapy rarely reverses the condition in men who have organic risk factors, whereas sildenafil therapy is usually successful.

The semantic question, then, is whether we can attach a name to these changes analogous to the term "menopause" used in women. The term menopause has evolved to mean a brief period during which the ovaries complete their evolution and cease to ovulate. Before that time, there is a variable period termed the "perimenopause," which some have divided into early and late phases. A few years after the last cycle, women enter the postmenopausal state. Men have no specific analogue to this narrowly defined menopause.

But changes with age in women do not relate solely to estrogen and progesterone levels. Muscle mass declines and fat mass increases from the 4th decade, just as in men. Alterations in cognitive function parallel those in men exactly, as do changes in mood and sense of well-being. The typical menopause in women, therefore, encompasses sets of changes whose relationship to reproductive hormone concentrations is tenuous. In men, a similar set of changes occurs whose relationship to hypogonadism and somatotropin deficiency remains unknown.

I dislike the term "male menopause" because of its reference to cyclicity, and I have adopted "manopause" as an umbrella term to describe age-related alterations whose exact nature is still to be determined. Perhaps this will cut the Gordian knot.

This, then, leaves the question of how we should define and treat hypogonadism in men. No evidence exists to indicate that older men need less testosterone than younger ones. In fact, studies suggest that because androgens induce their own receptors, tissues receiving inadequate amounts of testosterone will be more resistant to its effects than those more fully supplied. If bioavailable testosterone is what tissues respond to, then hypogonadism can be defined as a bioavailable testosterone level 2 or more SDs below the mean for young men (2.3 nmol/L in our laboratory's assay). Fasting morning values below this level are common in men older than 50 and increase progressively with age.

Many physicians avoid treating men who have mild hypogonadism, fearing the promotion of prostate cancer growth. There is no evidence that this occurs. Because our interventions to treat prostate cancer are aimed at reducing testosterone levels, the fear is that such therapy will boost androgen levels in men who may have subclinical cancer. But if a man has benign findings on a digital rectal examination and normal levels of prostate-specific antigen, these fears are unfounded.

The other problems with androgen therapy are erythrocytosis, possible promulgation of sleep apnea, and a reduction of high-density-lipoprotein (HDL)–cholesterol levels. These can all be easily monitored. In my practice, I usually give a hypogonadal man a 3-month trial of testosterone and then let him and his family tell me whether it was beneficial. If it was, the therapy is continued. To ensure that high enough HDL-cholesterol levels are maintained and that patients get the full benefit of treatment, I insist that they begin a substantial exercise regimen, including strength training. Currently I offer either a skin patch or self-injection therapy. A gel that can be applied to the skin will soon be available. Each treatment brings the plasma testosterone and bioavailable testosterone concentrations to the range of young men. Many men benefit greatly from therapy.

In the Public Eye

News and Features

US physicians may be failing to recognize substance misuse

Fred Charatan, Florida

A survey by the National Center on Addiction and Substance Abuse at Columbia University, New York, has found that 94% of primary care physicians may be missing or misdiagnosing alcohol-abusing patients.

Researchers presented a test case to a national representative sample of doctors. The case scenario stated, "A 38-year-old married patient has recurrent abdominal pain, intermittently elevated blood pressure, gastritis, and irritability, and wakes up frequently at night." Only 6% of physicians mentioned alcohol misuse as a possible diagnosis.

Richard Corlin, a California gastroenterologist, said that while the symptoms "are vague and common [and] can be related to a whole variety of conditions, they clearly indicate alcohol abuse, and doctors need to be made more aware of this possibility."

In the same survey, 41% of pediatricians failed to suggest drug misuse when presented with a classic description of a teenaged patient who is misusing drugs.

The survey of 648 primary care physicians, the most comprehensive so far, involved physicians in family medicine, general practice, internal medicine, obstetrics and gynecology, and pediatrics.

Doctors need to be more aware of this possibility

Only 19.9% of physicians felt that they were "very prepared" to deal with alcoholism, while only 16.9% felt very prepared to manage illegal drug use. In sharp contrast, 82.8% felt very prepared to identify hypertension, 82.3% to identify diabetes, and 44.1% to identify depression.

Although most physicians felt that medical treatment was effective for hypertension and diabetes, only 3.6% thought that it was effective for alcohol dependence and 2.1% for substance misuse.

The study also surveyed 510 patients being treated for substance misuse. Most (53.7%) said that their primary care physician did nothing about their addiction, 43% said that the physician never diagnosed it, and 10.7% said that the physician knew about it but did nothing.

Most physicians (57.7%) said that they do not discuss substance abuse with their patients because they believe their patients lie about it, and nearly 85% of patients agreed that they lie. More than a third (35.1%) of physicians cited time constraints as a reason for failure to discuss the issue, and 10.6% were concerned that they would not be reimbursed for the time necessary to screen and treat a substance-abusing patient. Less than a third of primary care physicians (32.1%) carefully screened for substance abuse.

The president of the center, Joseph A Califano Jr, who is a former US Secretary of Health, Education and Welfare, said,

> Substance abuse and addiction is the nation's number one disease. Primary care physicians must stop ignoring this elephant in their examining rooms. Medical schools, residency programs, and continuing medical education courses have an obligation to provide the training these physicians need to spot and deal with substance abuse.

Advice on how to screen patients for alcohol and drug misuse recently appeared in *wjm* (Cesar A Aristeiguieta: "Screening Patients for Alcohol, Tobacco, and Other Drug Misuse: the Role of Brief Interventions," January 2000, vol 173, pp 53-57).

California researchers receive highest number of FDA warnings

Fred Charatan, Florida

Of 22 warnings issued by the Food and Drug Administration (FDA) since 1999 for research violations, 9 were sent to California clinical researchers.

California received the highest number of warnings of any US state, according to a recent article in the *Los Angeles Times*. The warnings were for violations ranging from fraud to poor record keeping and lax supervision of junior researchers. Only 3 such warnings went to Texas and 2 to Wisconsin, and 8 other states received 1 apiece.

But David Lepay, director of investigations for the FDA's drug and research center, said that the number of warning letters issued was too low to draw any meaningful conclusions about the performance of individual states. "I frankly think that American clinical research is in very good shape," he said.

Many doctors who received the FDA reprimands complained that some of their studies began years ago, when standards were more lax, and that no patient in their studies was physically harmed.

Researchers who complain about the FDA's warnings often miss the point, said Theodore Friedmann, director of the gene therapy program at the University of California at San Diego. "The FDA exists to ensure not the well-being of the investigator, but of the patient."

An FDA inspection in March 1999 of a study by a contract research company, Irvine Center for Clinical Research, found that 1 or more study workers did not take the required temperature and respiration readings on 191 patients. Instead, they falsified readings and entered them in the records.

Ronald Cotliar, a Tustin dermatologist who headed the study, said through his attorney that the study coordinator who fabricated data had been fired and that patient safety was not compromised. He declined to name the treatment being tested or the company that sponsored the research, citing confidentiality agreements.

In another case in March 1999, Lawrence Dorr, an orthopedic surgeon at Good Samaritan Hospital in Los Angeles, received FDA clearance to import stainless-steel hip prostheses. He initially treated 46 patients with this experimental technique. The treatment was so successful that Dorr, without FDA permission, imported the prostheses from another overseas source to treat a further 40 patients on his own. Although he claimed he informed the extra patients of the device's experimental nature, the FDA charged that he obtained written consent from many of them only after the operation.

After Cotliar and Dorr undertook to improve practices and avoid future violations, the FDA closed their cases.

In a telephone interview, Peter Lurie, co-director of health research at Public Citizen in Washington, DC, criticized the FDA for inspecting only a small fraction of research studies. He said: "There's an enormous amount of sloppiness going on out there."

Lurie cited 3 main problems. First, there has been a vast expansion both in the US and internationally of contract research companies, which he called "HEX, or human experimentation, companies." Second, the close relationship between academia and industry has inevitably led to conflicts of interest. Finally, the shift of research away from academic centers has resulted in its fragmentation and decentralization and has led to studies of small patient groups at different sites, making quality control almost impossible.

Lurie said that Public Citizen would shortly publish a report on clinical research.

Gangrene bug killed 35 heroin users

Bryan Christie, Edinburgh

The likely cause of an infection that has killed 35 injecting heroin users in Britain and Ireland in recent weeks has been identified as *Clostridium novyi* type A, a bacterium only previously associated with serious infection during the two world wars.

An international effort to locate the source of the infection has isolated the bacterium from 9 infected drug misusers in Glasgow, and, although other cases are still being investigated, scientists are confident that they have now traced the cause of the deaths.

C novyi type A is present in soil and dust and is a well-recognized cause of infection in sheep, cattle, and other animals. It rarely poses a problem for humans in normal circumstances. Serious outbreaks occurred, however, during the first world war, when it proved to be the cause of 40% of cases of gas gangrene, and it also affected soldiers in the second world war.

"This is a case of an old bacterium finding a new niche in which to cause trouble as a result of a new form of human behavior," said John Hood, consultant microbiologist at Glasgow Royal Infirmary.

Scientists believe contaminated batches of heroin from a common source are responsible for the recent outbreak. The *Clostridium* bacteria in the heroin seem to have been able to survive being mixed with citric acid and heated—the process used to prepare the drug for injection.

All recent cases have occurred after injection into muscle, and, as these are anaerobic bacteria that grow only in the absence of oxygen, it seems that conditions were ideal for the bacteria to multiply and produce powerful toxins that have led to the deaths.

Brian Duerden, medical director of the Public Health Laboratory Service headquartered in London, said: "As far as we know, this is the first time this bacterium has ever

caused an outbreak of infection in drug injectors."

The first cases were reported in Glasgow at the beginning of May, and work in tracing the source has involved close collaboration between laboratories in Britain, Ireland, and at the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia.

Jai Lingappa, epidemic investigations officer at the CDC, said: "A lot more work still needs to be done to clarify how exactly the *Clostridium noyvi* is contributing to the illness. We are looking forward to the results of culturing the heroin under a variety of conditions to see if we can isolate the clostridia and other bacteria. We also want to learn more about why these people became sick and others didn't."

In all, 74 cases with the same clinical features have been reported so far, and there were no signs at the time of going to press that the outbreak was over. New cases were still being reported in Glasgow and in parts of England.

The investigators have no idea which heroin has been contaminated or how much of it has still to be used, and they have repeated advice to drug users not to inject.

California doctors' leaders sue health insurers

Fred Charatan, Florida

The California Medical Association (CMA) has filed an antiracketeering lawsuit against the state's three largest for-profit national health insurance companies. The CMA alleges that the health insurers Wellpoint/Blue Cross of California, HealthNet, and Pacificare have used coercive, unfair, and fraudulent means to dominate and control doctor-patient relationships for their own financial gain, to the detriment of patients and physicians alike.

The American Medical Association supports the action of the 30,000-member CMA, which alleges breaches of the federal Racketeer Influenced and Corrupt Organizations Act (RICO). The CMA's president, Marie Kuffner, hopes the lawsuit will be the last step in what has been an excruciating and lengthy effort to force the insurers' health plans to give physicians adequate resources to care for their patients.

"It is with sadness that we are forced to this last resort," said Kuffner, a professor of anesthesiology at the University of California in Los Angeles. "We, as physicians, have tried to work with the for-profit health maintenance organizations in the marketplace and have attempted to curb the abuses through the legislative process, all to no avail. We cannot continue to allow our patients' health to be jeopardized by corporate greed." She added: "For years these profit-driven companies denied needed services, interfered with medical decisions, and valued dollars more than lives. We say, 'No more in the state of California.' "

More than 9 million Californians, nearly 43% of those covered by for-profit plans in the state, are insured by the defendant plans. "CMA's role as plaintiff shows how crucial the health care problem is in the nation, particularly in California, where 21 million people belong to a managed care plan of some kind," said Archie Lamb, a lawyer in Birmingham, Alabama, who filed the suit on the CMA's behalf. The lawsuit uses the civil provisions of the RICO act to contend that the CMA's members have been harmed economically through a pattern of misconduct. If successful, the CMA may win up to 3 times the amount of damages that it would in a traditional lawsuit.

The insurers reject the CMA's charges and said that the action would only raise costs to the health care providers involved.

Global News Roundup

One in 6 children live in relative poverty

One in 6 children live below the national poverty line in their country, according to a new report from UNICEF. Rates of child poverty in the United States are higher now than they were in the 1970s, despite attempts at reforming the system of benefits for low-income families.

US might introduce abortion pill

The US Food and Drug Administration is considering approving the use of mifepristone (RU 486) to induce abortions, but only if used under strict conditions. Prescribing privileges may be restricted to doctors trained to perform surgical abortions, and clinics providing the service may have to be situated within 1 hour of an emergency room.

Chinese herbs may cause cancer

Doctors in Belgium have discovered that a Chinese herb, *Aristolochia fangchi*, already linked to renal failure, may cause cancer of the urinary system. The US Food and Drug Administration has sent a letter to US physicians with a list of herbal remedies thought to contain the hazardous herb.

New female condom to undergo trials

Scientists in Canada will undertake phase I trials of a new "invisible condom" for women. The condom is a gel, introduced into a woman's vagina, that acts first as a physical barrier to sexually transmitted pathogens and then kills them. It can also be used as a contraceptive when it includes spermicide. It is transparent, colorless, and odorless.

Medicare to cover patients in clinical trials

President Clinton has told the US Department of Health and Human Services to authorize payment for services covered by Medicare for patients in clinical trials. The directive, which does not require congressional approval, follows last December's Institute of Medicine report, which said: "Medicare should pay for routine care of beneficiaries enrolled in clinical trials in the same way it pays for this care outside of clinical trials."

Medicine and Money

The sum of my parts

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I worry of late that I am not as good looking as I used to be. I stopped exercising about a year ago after a move to the country. The bucolic setting disagrees with me. Recently, I turned 36 years old. But these aren't the bases for my complaint. The problem is that time has treated me more cruelly than others similarly situated. The rest of my birth cohort seems filled with vim and vigor. I, on the other hand, am fleshy, pallid, and prone to fits of profuse perspiration. This year, I vow to do something about it.

My first stop is my general practitioner, the best doctor I have ever had. "Stewart, this is the year I do it; tell me where I should start." He reminds me of visits around this time over the last 3 years when he talked me out of Prozac (1997), Viagra (1998), and an all-protein diet (1999). "I am way beyond all that. This is about releasing a happier me from a corporeal prison. A more beautiful me. A . . . " I go on at some length. Stewart suggests diet and exercise. "Impossible," I retort, "I am up for tenure in the Fall." He tells me that I'd have to gain a lot more weight before I am eligible to take a diet pill. I ponder this dilemma for some time. Then, in a flash, the answer comes to me: cosmetic surgery. Relief floods over me like warm butter.

The Web site www.medicineonline.com reads as if it was written just for me. The "Bid for Surgery" section of the site describes itself as an "E-exchange for cosmetic surgery, dentistry, ophthalmology, and podiatry." Inside is a virtual road map to bodily enhancement. Three dozen procedures are offered to stretch or snip my parts on cosmetic surgery's procrustean bed. I am to select one or more procedures, fill out a form detailing medical information, and then wait for the bids to flow in from practitioners across the United States. Narrowing the field of procedures is going to be a problem.

I decide to ask my life partner to select for me. A mistake. I get back a list of 8 procedures: Botox injections (for laughter lines—"Nothing's that funny," my partner says), correction of enlarged male breasts, eyelid surgery, liposuction, nose surgery, scar revision (long story), laser surgery for myopia, and teeth whitening (too much coffee while writing snappy commentaries). Clearly, we are going to need to set priorities. After a long heart-to-heart discussion, we settle on 4 procedures: eyelid surgery, liposuction, laser surgery, and teeth whitening. Sharing a quality moment, we fill out the forms together and on their completion pause, warmed by the glow of my computer's new flat screen monitor. We both sit transfixed by my image reflected by the digital surface. Somehow, I already seem slimmer, more beautiful. My partner's hand rests on mine as I click the left mouse key: "submit—register and request a bid." Yes, submit.

The bidding among the various specialists lasts for 7 days. In the meantime, I ponder the ethics of all this—it is, after all, my day job. In short, it is perfectly acceptable to auction cosmetic surgery services. The clearest I can make it is to compare it to prostitution. My favorite political philosopher, Michael Walzer, argues that the distribution of a good (be it sex or health care) is determined by its meaning for a particular society. "People who believe that sexual intercourse is morally tied to love and marriage are likely to favor a ban on prostitution. . . . Sex can only be sold when it is understood in terms of pleasure and not exclusively in terms of married love . . . " (*Spheres of Justice,* Basic Books,

Cosmetic surgeons can bid for customers on the Internet

1984). If you believe that cosmetic procedures in particular, or medicine in general, is a commodity, then you are committed to view free market forces on price, bidding, and unequal access based on wealth as wholly unproblematic. As Walzer says, "there is no such thing as a maldistribution of consumer goods. It just doesn't matter, from the standpoint of complex equality, that you have a yacht and I don't . . . " (p 108). Nose jobs are the aesthetic equivalent of yachts, and cosmetic surgeons who ply their trade on the Internet are the new captains of medical industry.

After a week, I had 4 bids on 2 procedures. Next time, I will have to say that I am willing to travel to California, the home of "Medicineonline.com." I ponder how to choose the right doctor: the most procedures per year, best patient ratings, fewest lawsuits, cheapest, or most expensive? I decide that the procedure I use for selecting sushi restaurants is most appropriate: pick the most expensive. Like raw fish, surgery should not be cheap. The cost for the new me? $6591. Of course, I have 6 more procedures to undergo. Sure it's a lot of money, but if I'm not worth it, who is? Of money—and he might have said the same of cosmetic surgery—the Bard said it is "that which makes the wappen'd widow wed again" (*Timon of Athens* IV:3).

At the time of this publication, Charles Weijer's photo was still being retouched

A Memorable Patient

My backbones

RS is a retired miner who comes down from his home in the mountains every few months for the treatment of rheumatoid arthritis. He has swollen joints and splinterlike spots around his fingernails from inflammation of tiny blood vessels. His immune system makes prodigious amounts of antibody against his own cells, a fact that worries me a little as I thumb through his medical record at each visit.

RS is easygoing and soft-spoken. Even when he is suffering, he always waits for his next appointment rather than seeing me sooner. Once in the examination room, he rarely complains. When I'm behind schedule, I know that a visit with this man of few words will be quick, enabling me to get back on schedule for my other patients.

Years ago, RS had severe leg pain from a herniated disc in his lumbar spine. I referred him to a neurosurgeon who decompressed the flattened nerve root. RS's leg pain resolved, but his back still hurts. Most of my patients, it seems, have a backache. When they describe their pain, my mind sometimes wanders. Like most rheumatologists, I'm more excited about extinguishing inflammation in swollen joints.

During a recent appointment, RS mentioned his back pain. I carefully palpated the joints of his hands and moved his other joints about. I took my glasses off to look closely at his nail beds and remarked that his rheumatoid arthritis and vasculitis were doing well.

As he made his way to the door, almost as an afterthought, I asked him to stand and bend forward. He slowly flexed his spine, and I heard the most horrible ratcheting, grinding noise. The sound softened as he straightened. Trying to stay calm, I asked him to bend again, and I again heard the ratchet, ratchet.

While he dangled his arms toward his feet, I took a moment for anxious reflection. Had a vertebra slipped forward, pulling on the spinal cord? Had I been shortchanging RS to spend more time with the complainers in my practice?

RS turned his head—by then, the veins of his face were bulging—and asked, "Can I straighten up now, Doc?"

"Please do," I managed to say.

I must have been pale because he asked, "Is something wrong?"

"Does your back always make those sounds when you bend over?" I asked.

He looked puzzled, then roared with laughter and pointed to a bulge in the pocket of his jeans.

"No, that sound came from these things rubbing against each other."

I felt such relief that, I'm embarrassed to admit, I let him leave the office without telling me what the "things" were. Later that day, I left a message on his answering machine, "What was in your pocket this morning?"

The next morning, I found a tin can filled with mints on my desk. Stuck to the can was a note from RS: "My backbones." I rolled the can in my palm. Sometimes life's messages come in small packages. The rattle of the mints reminded me to be truly present with patients, regardless of how forcefully they tell their stories.

I think I'll keep these mints in the examination room.

John Lynn, Colorado Springs, CO

Mail

Fatal asthma in a child after use of an animal shampoo containing pyrethrin

To the Editor,

An 11-year-old girl had been diagnosed with asthma at age 6 years. She had never been hospitalized and had rarely received steroids. Her only medication was albuterol, which was taken by inhaler as needed. On the day of admission, she gave her pet dog a bath using a shampoo containing 0.2% pyrethrin. She had used this shampoo 2 years earlier, with a brief but mild increase in her asthmatic symptoms that lasted 48 hours. The dog had been in the family home for several years. She was asymptomatic when she started to bathe the animal. Within 10 minutes, severe shortness of breath with wheezing developed, and she was immediately transferred to a hospital. She was intubated and treated aggressively for an acute asthmatic attack. She did not respond to treatment and died about 2-1/2 hours after the initial exposure to the pet shampoo.

At autopsy, there was mucous plugging of the bronchioles with an inflammatory infiltrate composed of neutrophils and eosinophils. There was prominent vascular congestion, and many alveolar spaces contained homogeneous eosinophilic edema fluid. The cause of death was listed as "respiratory arrest secondary to acute asthmatic attack." The pathology findings were consistent with the literature on pathologic changes in acute asthma.[1]

The pyrethrin class of insecticides was originally formulated from plants of the Compositae family, which includes daisies and chrysanthemums. Pyrethrum refers to both the crude plant extract and the marketed formulation of insecticide. Pyrethrin is the insecticidal chemical prepared from pyrethrum flowers, and it is also a market name for purified pyrethrum. A third term, pyrethroid, refers to insecticides of the same class, but these are synthetic compounds. Pyrethrum is known to cause allergy, including asthma and allergic skin disease. A review in 1934 warned physicians about its allergenic properties.[2] Our case is the first documented case of allergy to pyrethrin. No cases of pyrethroid allergy have been documented.

Neither pyrethrin nor pyrethroids are currently classified as allergens by the Environmental Protection Agency. Techniques of extraction from the flower have greatly improved the purity of the original pyrethrum formulations, and a recovery of 95% to 97% pyrethrin is now achievable.[3] The insecticide is, therefore, commonly marketed under the name of Pyrethrin, but it may contain small, but still allergenic, amounts of the impurities found in the crude extract. One suspected allergenic impurity is oleoresin, which may have been responsible for the allergic reaction in our case. The mechanism of allergy from pyrethrins is poorly documented. The marketing of pyrethrin is favored over that of pyrethrum, based on skin test studies suggesting that it is safer.[4] Although physicians have access to crude pyrethrum for skin testing, its purified isomers or mixtures of isomers are available only in the research laboratory. They are too expensive for practical use.

The possibility of an acute allergic reaction occurring from the use of any currently marketed pyrethrum insecticide should be considered in any case of respiratory or dermal allergy of unknown cause. This case suggests that physicians should also be alert to formulations marketed as pyrethrin. Pesticides of this class are being used with increasing frequency in homes and are easily available to the public. Manufacturers are not required by the Environmental Protection Agency to state on the label that the pyrethrum formulations are allergens.

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Marital status and physician-assisted suicide

To the Editor,

In the first 2 years that Oregon's Death With Dignity Act has been operative, 43 people legally obtained and used lethal prescriptions to end their lives.[1] Never-married and divorced persons were 4.2 and 3.2 times, respectively, more likely than married persons to use physician-assisted suicide. Unfortunately, the cross-sectional nature of the data precludes drawing any causal inferences from the findings. In addition, it is prudent not to draw any firm conclusions from such a small sample, and statistical analyses of so few cases are not particularly useful. Nevertheless, we give reasons why we believe never-married and divorced persons are more likely than married persons to take medication to end their lives.

Because most persons who have never married or are divorced are, by necessity, self-reliant, they may be devastated by any loss of their independence that accompanies a terminal illness. Thus, they may prefer to hasten their death rather than be overly dependent on others. Loss of autonomy and loss of control of bodily functions are strongly associated with physician-assisted suicide, and the vast majority of Oregonians who took the medication did so before becoming bedridden.[1]

According to a staunch opponent of physician-assisted suicide, people develop and maintain their sense of being valuable through relationships with others.[2] It should not surprise opponents, then, that the weaker family and social networks and greater likelihood of being lonely that never-married and divorced people have may make them less willing than married persons to tolerate living with a terminal illness. In a study of terminally ill Canadians, patients classified as having a serious desire for death had significantly lower levels of family support than other patients.[3]

Terminally ill single persons are probably less likely to receive assistance with everyday tasks, such as personal care and transportation, because they do not have a spouse to serve as their caregiver and, compared with married persons, they generally have less contact with their children. This may make their everyday life more difficult, thus increasing the likelihood that they hasten their death.

It should be easier for single persons to choose physician-assisted suicide because they do not have to consider the concerns of, or ramifications to, their spouse in deciding how to die. In addition, unmarried terminally ill elderly people are probably more susceptible to pressure (subtle and otherwise) to use physician-assisted suicide than married persons; con artists routinely target single elderly persons.

If physicians would ensure that their unmarried terminally ill patients were not isolated and received adequate assistance with their everyday needs, fewer persons would use physician-assisted suicide.

Dr Wineberg taught a course on physician-assisted suicide at Portland State University in 1998. M Purtzer was a graduate student in this course.

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Blaming the commentator

To the Editor,

Neither the word "blame," nor its concept, occurred anywhere in our qualitative study of pain treatment in people with sickle cell disease.[1] Even when identifying medical strategies involving mistrust, stigmatization, overcontrol, and neglect of sickle cell disease patients by health professionals, we avoided the simplistic idea of blame. So Morgan cannot have based his view that the study somehow "blames the patient"[2] on any words, tables, or figures in the text. Perhaps he was trying to read between the words or those of some subliminal subtext. This is not an advisable approach to a medical study, but it is undeniably useful as the basis for a good, if unsporting, rant about attitudes that play no part whatever in a piece of work.

We found that assertiveness, self-education, and an attitude of resistance to the disease were associated with a trend toward self-care at home. True, the words "assertiveness," "education," and "resistance" connote good things. However, we were unable to find any words to describe these phenomena that lacked such connotations: can we borrow Morgan's thesaurus? We reject the suggestion that to describe a person as educated and assertive about their condition is to "blame" another who cannot be so described. Rather, because knowledge of the disease and assertiveness can be taught, it is a call to sickle services to improve such support, particularly for affected children and families.

We agree that socioeconomic factors, including the "poverty and hopelessness" described by Morgan (admirably fearless of negative connotations here), are a severe obstacle to care in sickle cell disease and well worth a separate study. Our study steering group, comprising people with sickle cell disease and their advocates, did not think such data necessary to answer the specific questions this study asked. We remind readers that the study was performed in the United Kingdom where insurance status is not (yet, thankfully) a factor, and all National Health Service care is free at the point of use.

We agree that self-care of sickle pain requires access to strong oral opioids. This, in a framework of community support by a specialist nurse, is the model of care pursued by Dr David Bevan, 1 of the coauthors, who runs a clinical service. Inpatient care is also provided, predicated on whatever dose of parenteral opioid is needed to block the pain. Which bits of the text led Morgan to assume that we opposed good analgesia? We agree with everything he says on the subject, but he's aiming at the wrong target.

Supported home care with oral opioids has enabled 5 persons who previously spent more than 200 days per year in acute care wards to transfer to self-care for all but 20 to 30 days per year (D B). Because they still have the same pain pattern, their experience argues against frequency and intensity of pain being the solitary factors governing location of care. Every treater will also know affected persons who rarely come to hospital for their pain but have severe bone damage—aseptic necrosis, codfish vertebrae with collapse, bone-within-bone appearances on radiographs of long bones—indicating the cumulative effect of numerous sickle infarcts.

Such vignettes, along with our study and many other studies of pain in general, should guide clinicians away from a monolithic perception that pain is *either* a purely physical event *or* a cognitive and behavioral one: it is, of course, all of these and more besides. If Morgan's misrepresentation of our article encourages further study of this complexity, it was worth it.

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A Film to Make You Think

The Million Dollar Hotel directed by Wim Wenders; on worldwide release, 2000

What really distinguishes the US is the equanimity with which the majority contemplates the poverty of a minority.[1]

What remains to be wrested from experience when one has lost everything, and everyone, and there is no getting back into the world that was lost? These questions are difficult to answer in contemporary urban psychiatry. Yet, our patients face them every day. Sometimes this leads to despair or even suicide. Sometimes something "other" emerges that takes the observing physician by surprise.

In *The Million Dollar Hotel,* film director Wim Wenders brings his unflinching gaze to the subject of social exclusion. He focuses on a group of characters living in a squalid hotel in Los Angeles, each of whom lacks health insurance. Wenders often studies groups of protagonists, whether in a circus, the underworld, or a dance band. Most famously, in *Wings of Desire,* he gave us a portrait of angels who visited the libraries of Berlin to watch the city's inhabitants.[2]

In his other films, salvation was achieved through beauty. His new film slowly and honestly portrays awkwardness and ugliness. We watch the characters struggling to exist outside conventional society. They form an unfortunate distillate of brain-damaged, demented, addicted, psychopathic, or psychotic people. The subject matter will not appeal to all. At the screening I attended, a third of the audience left before the end. Yet, Wenders's film repays our attention. The mesmerizing final 10 minutes alone justify sitting through the slow opening. His conclusion, as so often in his work, is that life is beautiful. And, to Wenders's enduring credit, the viewer ends up concurring with this message.

The plot is simple. A resident dies by falling from the roof of the hotel. A mysterious private detective (played by Mel Gibson) arrives to investigate. We are not told how the residents, who live in poverty, could have afforded his fee. We gradually learn of his remit and of his own conflicts. Like many of the residents, he too, has experienced institutionalization.

Wenders revisits images ftom his earlier films—the death by falling in *Wings of Desire,* the ubiquity of modern surveillance techniques in *The End of Violence,* and the simultaneous view of many lives through many windows in *Beyond the Clouds,* which he codirected with Antonioni. He uses light and skies, and the natural, real time of human interaction. Crucially, his gaze remains on what many might find distasteful.

Finally, through a love story that evolves between a damaged man and a girl who may have autism or schizophrenia, Wenders concludes with a sacrificial act of enormous kindness.

Many psychiatrists will recognize an inherent truthfulness in this film. We see how dignity may exist amid squalor, exploitation, and exclusion. Some of the actions portrayed in this film lack coherence, but then, that may be true of life. Either way, it is no less beautiful.

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Original Research

Ionization and photoelectric smoke alarms in rural Alaskan homes

ABSTRACT **Objective** To compare rates of nuisance alarms and disconnection between ionization and photoelectric smoke alarms. **Design** A prospective cohort study. **Setting** Four Inupiat Eskimo villages in the Northwest Arctic Borough region of Alaska, 48 km (30 mi) above the Arctic Circle. **Subjects** Households in 4 communities with similar populations, number of homes, mean income, size of household, and square footage per home. **Intervention** Two villages had photoelectric alarms installed (58 homes), and 2 other villages had ionization alarms installed (65 homes) in standard locations. Follow-up household surveys were conducted after 6 months to determine rates of false alarms and detector disconnection. All of the households that could be contacted 104/123 agreed to participate in the follow-up surveys. **Main outcome measures** The proportion of households experiencing false alarms and the proportion of disabled alarms in households in each of the test communities. **Results** Homes with ionization alarms had more than 8 times the rate of false alarms as those with photoelectric alarms. Eleven of the ionization alarms (19%) were disconnected compared with 2 of the photoelectric devices (4%). **Conclusions** In small rural residences, photoelectric smoke alarms have lower rates of false alarms and disconnection. Photoelectric alarms may be the preferred choice for dwellings with limited living space or frequent false alarms.

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Between the years 1986 and 1995, an annual average of 5,000 people lost their lives and another 28,000 were injured in US fires.[1(p2)] The problem for Native Americans is even worse, with a fire fatality rate that is 3.6 times higher than the national rate of 1.28 per 100,000 people.[2] Alaska has the highest fire fatality rate among states in the United States.[3] The fire fatality rate for Native Alaskans (12.3/100,000) is 9.6 times the national rate and 3.5 times higher than the Alaska rate for all races of 3.47 per 100,000.[4] For the 19 Alaska residential fires involving 23 deaths in 1996, only 5 homes (26%) had a smoke alarm installed, and only 1 of them (5%) was operational at the time of the fire.[5] Most rural Native Alaskans live in small homes with electrical heating systems that do not meet accepted industry standards. When the fact that most rural villages have little or no fire-fighting capabilities is added, the potential for disaster is great. This situation is not unlike that seen in other poor rural US communities, mobile home parks, and some apartment complexes. Therefore, early detection and escape become essential elements in preventing fire fatalities among these populations.

A working smoke alarm has been reported to reduce the risk of death from residential fires from 50% to 70%.[6,7] There are basically 3 different types of residential smoke alarms: the ionization alarm, the photoelectric alarm, and the combination alarm. The US Fire Administration reports that more than 88% of the homes in the United States have at least 1 smoke alarm installed, but 60% of the residential fire deaths occur in homes without an operational alarm.[8] According to a 1994 study of US residential smoke alarm use, the leading cause of smoke alarm disconnection was nuisance alarms.[9] Frequent nuisance alarms can generate a dangerous sense of complacency, resulting in needless fatalities. Once disconnected, a smoke alarm is rarely reconnected, leaving residents at increased risk of injury or death from fires.

Consumers Union tested ionization and photoelectric alarms in 1994.[10] It found that in a smoldering, smoky fire, the ionization alarms responded in 25 to 35 minutes, whereas the photoelectric models reacted in half that time.

The US Fire Administration's data show that the number 1 cause of fire fatalities in the United States is careless smoking.[1(p6)] Hall and Harwood showed that about 70% of the fire deaths in the United States each year are a result of smoke inhalation rather than burns.[11] Slow, smoldering fires, such as those from cigarettes igniting a mattress or couch, are the types most commonly associated with residential fire fatalities, yet the ionization alarms that are found in 87% of US homes are more sensitive to flaming-type fires.[12]

In this prospective cohort study, we installed smoke alarms in Alaska Native village homes to compare the frequency of false alarms and the disconnection rates between ionization and photoelectric alarms. We hypothesized that photoelectric alarms would be associated with lower rates of nuisance alarms. If one type of alarm has a lower rate of false alarms, then long-term functional capability may be improved. Physician warnings and counseling of patients have been shown to be effective in creating beneficial changes in behavior.[13] Clinicians can have a tremendous effect on their patients' safety by counseling them on the use of smoke alarms, especially alarms that fit the patients' lifestyles and home environments.

METHODS

This was a prospective cohort study of households in 4 rural Alaskan villages. The outcomes of interest were

the false alarm and disconnection rates of ionization compared with photoelectric smoke alarms. The geographic area chosen for this research was 48 km (30 mi) above the Arctic Circle in the Northwest Arctic Borough of Alaska. This area spans 36,000 sq mi and is inhabited by 12 Inupiat Eskimo villages with a total population of about 6,500. Resources were available to study only 4 of the 12 communities in this region of Alaska. Selection of the 4 villages was based on comparability among villages in the number of homes, the square footage per home, population, and average income. Villages, rather than homes, were assigned to 1 of the 2 groups. Random assignment of homes was not considered because of ethical concerns expressed by village leaders. Two of the communities received ionization alarms, and 2 received photoelectric alarms, with 1 village from each category being randomly selected from 2 distinct geographic regions. This was thought to prevent possible cross-contamination in which residents might express preferences for 1 alarm over another. Most of the homes in this region contain less than 93 m^2 (<1,000 sq ft) of living space, and most of these villages have no fire-fighting capabilities, other than water buckets and portable fire extinguishers. All smoke alarms were provided free to residents through the Injury Prevention Program of the Alaska Native Health Service. All of the ionization alarms were 1 brand and model, as were all of the photoelectric alarms.

As a result of the baseline survey, only homes that were not built as part of a US Housing and Urban Development (HUD) project were selected to receive smoke alarms. The HUD homes were deselected because they had smoke alarms connected directly to the electrical circuits. The estimated number of homes needing smoke alarms was determined through the administrative office in each village. Two weeks before installation, the project and installation dates were advertised to residents in each of the villages using posters, citizens-band radios, and local radio stations.

The investigator and a village representative then went to each house gathering baseline data, testing existing alarms, and installing new alarms. All of the residents granted permission for this inspection, but of the 148 homes initially surveyed in the 4 villages, 25 (17%) were excluded because they had alarms that were wired into the electrical system. Baseline data were collected on any existing smoke alarms by pushing the test button and by spraying aerosol smoke into the sensing chamber to activate the alarm. If no alarm sounded, a visual inspection was conducted for the presence of a battery. Regardless of the presence or absence of a functioning smoke alarm, residents were given the opportunity to have a new alarm installed.

In the 123 homes where new alarms were installed, smoke alarms were mounted on the ceiling about 3 to 4.6 m (10-15 ft) from the cooking and the heating sources. The average distance for smoke alarm installation in the ionization group was 4 m (13 ft) from the heating source and 4.3 m (14 ft) from the cooking source. In the photoelectric group, the average distance from the heating source was 4.6 m (15 ft) and 4.4 m (14.5 ft) from the cooking source (table).

During the baseline survey, functioning smoke alarms were found in 32 (38%) of 85 homes in the ionization group compared with 14 (22%) of 63 homes that would become the photoelectric group. Sixty-five homes (76%) in 2 of the villages received installation of ionization alarms, and 58 homes (92%) in the other 2 villages received photoelectric alarms.

Residents were given instructions on smoke alarm maintenance, testing procedures, how to change batteries, and how to use the "hush button" if one was present (ionization alarms only). After installation, each smoke alarm was fogged with an aerosol "smoke" to test the audible alarm. Residents were also asked to document each time their smoke alarm sounded its alarm and the reasons.

A 6-month follow-up survey was attempted at each participating home by the investigator and a village representative. The homeowners had been told to expect a 6-month follow-up visit, but the exact date was unannounced. Residents were asked if they had experienced false alarms from their smoke alarms. If false alarms were experienced, they were asked how many occurred, what were the causes, and how were the alarms silenced. Smoke alarms were tested and re-fogged during this follow-up visit to verify their operability.

RESULTS

Of 311 homes from the 4 villages, 148 were included in the study at baseline. Attempts were made to contact all 123 participants during the 6-month follow-up survey,

Summary points

- Functioning smoke alarms can reduce the risk of death in residential fires from 50% to 70% each year
- Of the residential fire deaths in the United States, 60% occur in homes without a functioning smoke alarm
- Smoke alarms are often disconnected because of frequent false (nuisance) alarms
- Higher rates of false alarms seem to be associated with small dwellings, use of wood fuel for heat, and location of alarms near cooking areas
- Photoelectric smoke alarms have a lower rate of false alarms and subsequent rates of disconnection than do ionization alarms
- Patients should be informed about the advantages of photoelectric smoke alarms in dwellings that have frequent false alarms

Comparability of villages by type of smoke alarm

Variable	Photoelectric alarm Village A	Photoelectric alarm Village B	Ionization alarm Village C	Ionization alarm Village D
Population, No.	298	416	575	249
Older/total homes	33/71	30/58	40/115	45/67
Persons/home, mean No.	4	7	5	4
Footage/home, mean m² (mean sq ft)	88.6 (954)	85.9 (925)	101.3 (1,090)	90.6 (975)
Annual income, mean, $	<20,000	<20,000	<25,000	<20,000
Distance from alarm, mean m (ft)				
Heating source	4.0 (13)		4.6 (15)	
Cooking source	4.3 (14)		4.4 (14.5)	

but 19 were unavailable (85% completion rate). At the end of the 6-month study period, 48 (81%) of 59 homes in the ionization group had functioning alarms compared with 43 of 45 homes (96%) in the photoelectric group. Fifty-four (92%) of the homes with ionization alarms had at least 1 false alarm compared with 5 (11%) of the homes in the photoelectric group. Of the 69 false alarms experienced by the ionization group, 64 (93%) were reported to be related to cooking, compared with 4 of 6 (67%) in the photoelectric group. Frying accounted for 52 (81%) of the 64 cooking-related false alarms. The heating source was the second most-common cause of nuisance alarms, accounting for 5 (8%) of 64 in the ionization group and 2 of 6 (33%) in the photoelectric group.

Eleven homes in the ionization group had nonfunctioning alarms, and the leading reason (9/11) given for disconnecting these alarms was that "it goes off too much." The other 2 ionization alarms contained dead batteries. Although 2 alarms were disconnected in the photoelectric group, neither was related to nuisance alarms. The reasons given for disconnection were to use the battery in a toy, and the other was inadvertently knocked down while changing a light bulb.

DISCUSSION

This study demonstrates that in the test communities, ionization smoke alarms were almost 5 times more likely to be disconnected 6 months after installation compared with photoelectric alarms. It appears that this marked difference in disconnection rates is due to the 8-fold higher incidence of nuisance alarms in homes with ionization alarms. Other studies have also found that nuisance alarms are an important cause of disconnection with ionization alarms.[6,14(p12)] However, we are unaware of other community-based studies that have demonstrated that photoelectric alarm installation is associated with a substantially lower rate of disconnection. These findings have possible significance for the public health and the fire safety community because 1 of the barriers to improved fire protection is the maintenance of smoke alarms already installed in homes. Replacing ionization alarms in household areas prone to nuisance alarms with photoelectric alarms could potentially lead to a marked reduction in the proportion of disconnected alarms. This research should be useful for any dwelling in which frequent false alarms are experienced or in dwellings with less than 93 m² (<1,000 sq ft) of living space. These criteria are by no means unique to rural Alaska.

Research on Native American smoke alarm use and experience is sparse. A 1996 survey of 80 households on the Devil's Lake Sioux Reservation in North Dakota reported that 79% of the 109 ionization smoke alarms installed had false alarms during the previous year.[15] Of the homes experiencing false alarms, almost half had more than 25 alarms per smoke alarm. Because of these nuisance alarms, 49% of the alarms had been disconnected over the previous year. Only 3 of the 112 alarms in the Devil's Lake study were photoelectric, none of which had a nuisance alarm reported.

The fact that ionization alarms produce more false alarms but are slower to respond to smoky fires is not the enigma that it seems. Smoke from cooking tends to contain smaller particles (<1 μm) that will activate the ionization alarms, whereas larger smoke particles are necessary to activate the photoelectric alarms.[8] A possible barrier to the increased use of photoelectric alarms is their higher cost (about $20), which is roughly double that of the ionization alarms. New alarms featuring both types of sensors in 1 unit are currently available but, if located too close to the kitchen or other ignition sources, nuisance alarms could still be a problem.

This study has several limitations. First, we are uncertain about the generalizability of our findings. Factors such as housing size, cooking practices, crowding, and air exchange may all play a role in increasing the likelihood of nuisance alarms. It is unclear if similar findings would be

encountered if this study were replicated in a middle-income community with a larger average house size. Another limitation of the study was the baseline differences in the village groups before installation of the alarms. The groups receiving photoelectric alarms were less likely to have alarms at baseline.

Bias may have potentially affected the results in 2 ways. First, recall bias may have influenced respondents' answers regarding alarms. Those who experienced more alarms may have been more likely to recall their occurrence than those experiencing fewer alarms. However, it is unlikely that differential recall bias existed between groups and highly unlikely that the magnitude of difference between groups could be explained by recall bias. A larger proportion of the homes in the photoelectric group were also unable to be recontacted, which may have led to differential bias in the outcome measurements between groups. However, if every household that could not be contacted in the photoelectric group had experienced nuisance alarms (18/58, or 31%), the magnitude of difference between groups would still be an absolute difference of 61%.

Homes in the 2 village groups may have differed in some unmeasured dimension that could have influenced the rate of disconnection or nuisance alarms. This is unlikely given that the homes, cultural profiles, and socioeconomic status of the 4 villages were virtually identical. Furthermore, the distance of the alarms from possible ignition sources was standardized between groups. The primary reason given for false alarms was "cooking," and the average distance differential between the 2 groups was only 15 cm (6 in). Finally, neither the occupants nor the investigators conducting the outcome assessments were blinded by the type of device installed in the home. This can lead to differential ascertainment bias between the groups.

We conclude that the incidence of nuisance alarms is much higher in small dwellings using ionization smoke alarms. The higher rates of alarm disconnection in the homes with ionization alarms are likely related to the high rate of nuisance alarms in these homes. The use of photoelectric smoke alarms in small dwellings may lead to a lower rate of disconnection and improved survival in the event of fire. Randomized controlled trials comparing these types of alarms in different types of dwellings should be conducted to confirm these findings.

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COMMENTARY

Smoke alarms and prevention of house-fire–related deaths and injuries

Smoke alarms have saved thousands of lives in the United States since their introduction and widespread use during the past 2 decades. The good news is that more than 90% of homes in the United States now have at least 1 smoke alarm.[1] The bad news is that a substantial proportion of those smoke alarms do not work. In on-site surveys of homes with smoke alarms, about 25% to 30% of the alarms did not function when tested.[2] Some failures are due to malfunction of the alarm itself, some are due to a dead battery, and some do not function because the battery has been removed.[2,3] The study by Fazzini and colleagues is particularly relevant for the last group.

The authors compared the rate of false alarms (or "nuisance alarms") between ionization-type and photoelectric-type smoke alarms that had been installed in low-income homes in 4 small villages in Alaska. Six months after installation, more than 90% of the homes with ionization-type alarms had experienced false alarms, mostly from cooking, and 19% had been disconnected, presumably because of the nuisance alarms. The comparison group

with photoelectric alarms had low rates of nuisance alarms (11%) and battery removal (4%). Whereas these differences are statistically significant and important, the data should be interpreted with caution because of the unique nature of the population studied. The rates of nuisance alarms and battery removal found in Alaska are severalfold higher than previously seen[4] and may be due to several unusual characteristics of this population in Alaska and the methods used in the study.

The homes in the study were small, averaging less than 1,000 sq ft of living space. As a result, the distance between the kitchen and the alarm was short, a factor known to increase the chance of a nuisance alarm from cooking.[5,6] In addition, most of the nuisance alarms were due to frying, which results in more smoke than other forms of cooking. If the practice of frying food was more prevalent in the villages with ionization-type alarms, this could have accounted for much of the difference between the 2 groups, with the difference being magnified by the proximity of the alarm to the kitchen. In addition, differences in the presence of effective exhaust fans may have influenced the rate of false alarms.

Another unusual finding from the study is the high proportion of the homes in which the alarm battery had been removed, even though the incidence of nuisance alarms appears to have been an average of only slightly more than 1 per home (69 nuisance alarms in 54 homes, with at least 1 nuisance alarm). The authors report that the alarms had silence buttons that disable the alarm for 10 minutes, allowing the smoke to be cleared; yet, the batteries were removed. This raises the question of whether the people in the homes with these alarms knew how to silence them. In our experience, some alarms are difficult to silence without specific knowledge of where to press on them and how long to press to silence them. Perhaps better instruction about the method of silencing the alarm would decrease the chance of battery removal for nuisance alarms in this setting.

These issues are important because photoelectric alarms cost almost twice what ionization alarms cost, so only half as many homes can be protected within a given budget. The findings of Fazzini and colleagues need to be confirmed and replicated in other populations to weigh the relative costs and benefits of ionization against photoelectric alarms.

Smoke alarms will probably continue for the foreseeable future to be one of the most important means of preventing fire-related deaths. Homes at highest risk of fire and fire-related deaths and injuries are those least likely to have smoke alarms—that is, homes in the lowest socioeconomic neighborhoods and those of substandard quality.[7,8] Identifying those homes and ensuring that they have smoke alarms installed are challenging public health issues. Systematic use of surveillance data to identify deaths and injuries due to house fires is essential to focus resources into neighborhoods at greatest risk and where the greatest benefit may be inured. Once identified, these areas can be the target of efforts to increase the prevalence of smoke alarms, such as through mass smoke alarm distributions.[4,9-11]

The opportunity exists to mobilize our collective efforts with the goal of eliminating deaths related to house fires in the United States. A multifaceted approach to elimination should include the distribution of smoke alarms, education about fire prevention, legislation to require smoke alarms in all existing residences and fire sprinkler installation where possible, enforcement of existing codes, and development of new and better long-lived smoke alarms. Such an approach can take us well along the road to eliminating deaths related to house fires.

Primary care physicians can play an important role in this preventive effort in at least 2 ways.[12] First, physicians can educate patients about the importance of fire prevention, escape plans, and smoke alarms, including issues about nuisance alarms and how to deal with them. Second, physicians can advocate for a community-based approach to try to reach those persons at greatest risk through programs such as smoke alarm distributions. Through a collaborative approach among physicians, public health agencies, fire departments, private industry, and volunteer groups such as the Red Cross, house-fire–related deaths may one day become as rare as some vaccine-preventable diseases.

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Exposure to electromagnetic fields and suicide among electric utility workers: a nested case-control study

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ABSTRACT **Objective** To examine mortality from suicide in relation to estimated exposure to extremely low–frequency electromagnetic fields in a cohort of 138,905 male electric utility workers. **Methods** Case-control sampling, which included 536 deaths from suicide and 5,348 eligible controls. Exposure was classified based on work in the most common jobs with increased exposure to magnetic fields and indices of cumulative exposure to magnetic fields based on a measurement survey. **Results** Suicide mortality was increased relative to work in exposed jobs and with indices of exposure to magnetic fields. Increased odds ratios (ORs) were found for years of employment as an electrician (OR, 2.18; 95% confidence interval [CI], 1.25-3.80) or line worker (OR, 1.59; 95% CI, 1.18-2.14), whereas a decreased OR was found for power plant operators (OR, 0.67; 95% CI, 0.33-1.40). A dose-response gradient with exposure to magnetic fields was found for exposure in the previous year, with a mortality OR of 1.70 (95% CI, 1.00-2.90) in the highest exposure category. Stronger associations, with ORs in the range of 2.12 to 3.62, were found for men younger than 50 years. **Conclusions** These data provide evidence for an association between occupational electromagnetic fields and suicide that warrants further evaluation. A plausible mechanism related to melatonin and depression provides a direction for additional laboratory research and epidemiologic evaluation.

In the United States, suicide is currently the 8th leading cause of death[1] and is, with homicide, the third leading cause of years of potential life lost.[2] Although suicide rates showed a steady increase from the mid-1950s to the late 1970s, they have changed relatively little during the past 15 years. Mental and addictive disorders are the key risk factors for suicide and suicidal behavior.[3] Analyses of patterns and trends of suicide in the United States show increased risks among people who are male, white, divorced or widowed, elderly, and those living in western states.[3,4]

The potential for an association between extremely low–frequency electromagnetic fields (EMFs) and suicide is biologically plausible. Wilson has postulated a link between exposure to EMFs and depression, based on observations that these exposures alter the daily rhythm of pineal melatonin production and excretion in rats.[5] A pathway involving the effect of EMFs on the production of melatonin, the role of melatonin in depression, and depression as an important risk factor for suicidal behavior points to suicide as a possible consequence of exposure to EMFs. Although data concerning the effects of exposure to EMFs on human pineal function are limited, inhibition of melatonin production has been reported.[6-8] Furthermore, in several reports, lower levels of melatonin formation are associated with depression.[9-12] Moreover, exposure to EMFs has been linked with depression and depressive tendencies.[13-18] Finally, there is strong evidence that depressive illness is an important risk factor for suicide.[3,4]

We conducted a case-control study to consider the risk of suicide for electric utility workers for whom individual estimates of exposure to magnetic fields were obtained based on job titles. The study population of 5,884 subjects was obtained from a cohort of 138,905 men in the original mortality study.[19] Knowledge about the relation between exposure to magnetic fields and suicide is extended through the analysis by time windows, distinguishing possible acute and chronic effects of exposure. Also, analyses were performed for separate age categories. People in different age categories may be more or less vulnerable to the effects of exposure to EMFs because the nature of depression seems to change with age.[20,21]

METHODS

Design and study population

Details of the cohort identification have been published elsewhere, and the cohort is briefly described here.[19] Eligible workers were employed full-time at any of 5 electric power companies in the United States at any time between January 1, 1950, and December 31, 1986, with a total of at least 6 months of continuous employment. Women were excluded because they rarely worked in jobs with the exposure of interest. After exclusions due to lack of availability of records before September 1, 1954, and January 1, 1955, at 2 of the companies, missing date of birth, unknown starting dates, and other errors in the records, 138,905 workers were included in the cohort.

The case-control sampling from the original cohort included all 536 deaths from suicide (*International Classification of Diseases,* 8th and 9th revisions, codes E950-E959) and 5,348 eligible controls. Controls were selected with the use of risk-set sampling.[22] For each suicide case, workers in the cohort who were alive on the date of death of the case-person and who had the same birth year and

ethnicity were matched. If fewer than 10 eligible controls were available for the case, then all eligible controls were selected; otherwise, 10 were randomly chosen. This selection procedure generated for each case a set of controls that provided an estimate of the population distribution of exposure at the time of the case-person's death.[23]

Assignment of exposure to magnetic fields

Workers in the electric utility industry have complicated patterns of exposure to EMFs, with several possible measurements, including transient measures of magnetic and electric fields.[24,25] Exposure to EMFs was estimated by an assessment of exposure to magnetic fields, focusing on the time-weighted average, as described in detail elsewhere and briefly summarized here.[19,26-28]

Complete work histories were abstracted and computerized. To consolidate thousands of job titles at the 5 participating companies, 28 occupational categories were constructed based on work activities, responsibilities, and exposure potential[26] to define the rows of a job exposure matrix. Within the occupational categories, 1,060 distinct job titles were monitored. Randomly selected workers wore a personal average magnetic exposure meter (AMEX; Enertech Consultants, Campbell, CA) that recorded the time-integrated mean exposure to magnetic fields over the work shift. A total of 2,842 usable measurements was obtained and used to compute time-weighted average exposures and arithmetic means for each occupational category in the job exposure matrix.[27,28] Cells for exposure to magnetic fields were rank ordered and collapsed into 5 groups to increase statistical precision. Grouping was based on the distribution of the arithmetic mean exposure of each occupational category measured successfully in each company. The 25, 50, 75, and 87.5 percentiles were chosen as arbitrary cutoff points to arrive at 5 groups (5-level job exposure matrix), with time-weighted average exposures of 0.12, 0.21, 0.39, 0.62, and 1.27 μT. Each of the combinations of company and occupational category was placed in 1 of the 5 levels of the job exposure matrix according to the estimated level of exposure to magnetic fields.[28] The average group exposures were assigned for each occupational category and summed over employment intervals for each worker. The mean exposures in each calendar year were summed and multiplied by the proportion of all hours spent at work (0.23) to yield workday exposure in microtesla-days and divided by 365 to yield microtesla-years of occupational exposure.[19]

Confounding factors

Established risk factors for suicide are a history of mental and addictive disorders, abnormalities and alterations in the serotonin system, and disrupted family environment.[3] However, information on these confounding factors was not available from personnel records at the companies. Socioeconomic status,[29,30] solvent exposure,[31] decreased exposure to sunlight,[32-34] and living in the western United States[3,4] are possible risk factors for suicide and were taken into account in this study.

Workers were classified into 4 categories of social class: upper white collar, lower white collar, skilled blue collar, and unskilled blue collar workers. Possible exposure to solvents was assessed by expert panels at each of the 5 participating companies. Solvents were used as thinners, degreasers, cleaners, and lubricants and included 1,1,1-trichloroethane, acetone, carbon tetrachloride, and Varsol. Workers were classified as unexposed to an agent up to the time when they entered a job with exposure potential, and they remained classified as exposed thereafter.[19,35] For exposure to sunlight, workers were classified in a similar manner. Panels classified each job as involving primarily indoor or primarily outdoor work. Information on occupational exposure to sunlight was collected only at the 3 largest companies; therefore, exposures at the 2 smaller ones were estimated.[35] The 5 participating electric utility companies were divided into 2 groups, depending on their location in the United States. One company was located in the western United States, and the other companies were in the eastern United States.

Data analysis

First, the association with exposure to magnetic fields was investigated using occupational categories. Suicide risks were considered for electricians, line workers, and power plant operators, the 3 most common jobs with increased exposure to magnetic fields among the 5 utility companies.[19] Risk estimates were calculated for men in those occupations during the calendar year of death who were ever employed as such in the 1- to 5-year period before death and for men with the specific occupations as the longest held job throughout their career. The reference group consisted of those not employed in the category of interest in the specific time intervals.

As well as the analyses with occupational categories, risk estimates were assessed based on time-integrated exposure. Cumulative exposure (microtesla-year) in the calendar year before the year of death (past 1-2 years) was considered recent exposure. Total exposure was assessed as career exposure for cases and cumulative exposure up to the date of death of the matching case-person for controls. Furthermore, cumulative exposure was examined in 4 time intervals: past 1 to 5 years before death, past 5 to 10 years before death, past 10 to 20 years before death, and 20 years or more before death. The time windows were chosen to consider possible latency of the effect of exposure to magnetic fields on suicide.

For recent and total exposure and for each of the 4 time windows, exposure categories were created based on percentiles of exposure of cases, ensuring an equitable dis-

Table 1 *Crude conditional logistic regression odds ratios (ORs) (95% confidence intervals [CIs] for suicide relative to potential risk factors*

Risk factor	Controls No. (%)	Case-persons No. (%)	OR (95% CI)
Work			
In work	2,865 (93.0)	215 (7.0)	1.00
Out of work	2,483 (88.6)	321 (11.5)	2.15 (1.75-2.66)
Social class			
Upper white	728 (91.9)	64 (8.1)	1.00
Lower white	771 (90.0)	86 (10.0)	1.27 (0.91-1.78)
Skilled blue	2,069 (90.5)	217 (9.5)	1.19 (0.89-1.59)
Unskilled blue	1,780 (91.3)	169 (8.7)	1.07 (0.79-1.46)
Exposure to solvents			
No	1,483 (91.0)	146 (9.0)	1.00
Yes	3,865 (90.8)	390 (9.2)	1.03 (0.84-1.25)
Exposure to sunlight			
No	2,824 (91.8)	254 (8.3)	1.00
Yes	2,524 (90.0)	282 (10.1)	1.25 (1.04-1.50)
Location in United States			
East	3,251 (60.8)	272 (50.7)	1.00
West	2,097 (39.2)	264 (49.3)	1.56 (1.30-1.89)

tribution of deaths across categories. For acute exposure and the 4 windows, 0 exposure was chosen as the referent category (men who were not employed in the relevant time window) and compared with men in quartiles of that distribution. For chronic exposure, men below the 25th percentile formed the referent category, with the other percentiles defined as 25 to 49, 50 to 74, 75 to 89, and 90 or greater. Suicide risk was also evaluated among men in 3 different age categories (≤34 years, 35-49 years, and ≥50 years). Here also, 0 dose was chosen as the referent category and compared with men in percentiles of 0 to 49 and 50 or greater, based on the distribution of exposure of cases.

Adjusted odds ratios (ORs) (estimated rate ratios) and 95% confidence intervals (95% CIs) were derived from conditional logistic regression models with a proportional hazards regression procedure of commercial statistical software (SAS system, version 6.12; SAS Institute, Cary, NC). These analyses were conditioned on the matching factors birth year and ethnicity. Work status, reflecting whether a worker was or was not employed in a given year of death, was included in the model to control for the healthy worker effect,[36] which was important for the outcome of suicide. For consistency, social class, location of company, exposure to solvents, and exposure to sunlight were also included in the model, although little confounding by these variables was found.

RESULTS

Mortality from suicide was similar to overall mortality in the original cohort with respect to race and calendar year.[19] Nearly 87% of the men who committed suicide were white, and most deaths occurred in 1980 to 1988. The average duration of work was 16.2 years (SD 9.8 years). Nevertheless, compared with the overall mortality in the original cohort, the age distribution of suicide deaths was different. The average age of the case-persons was low: 49 years, ranging from 19 to 93 years. Fifty-three percent of all suicide deaths occurred before age 50. Of the 3,502 deaths in this age group in the original cohort, 286 (8.2%) were due to suicide.

Table 1 presents ORs for potential risk factors for suicide available in this study. Being out of work, exposure to sunlight, and location in the western United States were all associated with suicide. Men who were out of work had about a 2-fold increased risk of committing suicide compared with active workers. Exposure to sunlight at the workplace seemed related to a modestly increased risk for suicide (OR, 1.25; 95% CI, 1.04-1.50). Workers living in the western United States had an OR of 1.56 (95% CI, 1.30-1.89). Social class and exposure to solvents were not related to suicide.

Table 2 shows the risk for suicide among men working as an electrician, line worker, or power plant operator at 3 different periods: during the calendar year of death, during 1 to 5 years previously, and throughout a career. Increased risks were found for employment as an electrician in all 3 periods, strongest for the most recent periods. Employment as a line worker also increased the risk, but not in the past year. Employment as power plant operator was weakly inversely associated with suicide.

Table 3 shows the risk estimates for suicide relative to cumulative exposure to magnetic fields in several timeframes. A monotonic dose-response gradient was found, with recent exposure as a categoric measure and an OR of 1.70 (95% CI, 1.00-2.90) in the highest interval. For cumulative exposure in the past 1 to 5 years before death, the categoric analysis yielded ORs of 1.12 to 1.53. Although the dose-response gradient was inconsistent, the highest risk was in the group with the highest exposure. For the other windows of exposure, the ORs were close to or below the null, providing no indication of increased risks. A weak inverse gradient in risk occurred with increasing exposure for a cumulative exposure of 20 years or more before death. For total exposure, increased ORs were found for all levels above the referent, but there was no dose-response pattern.

Men younger than 50 years with recent exposure above the median had notably higher ORs: 2.39 (95% CI, 1.00-5.69) for men younger than 35 years and 3.62 (95% CI, 1.41-9.29) for men aged 35 to 49 years (table 4). Men aged 50 years and older had ORs of less than 1.00, but this group included retired workers without recent exposure. However, restricting the analysis to men aged 50 to 66 years provided similar results. The ORs were lower for cumulative exposure in the period 1 to 5 years before

Table 2 *Adjusted* conditional regression odds ratios (ORs) (95% confidence intervals [CIs]) for suicide relative to type or duration of work in selected occupations*

Time of employment†	Electrician, No. Cases	Controls	OR (95% CI)	Line worker, No. Cases	Controls	OR (95% CI)	Power plant operator, No. Cases	Controls	OR (95% CI)
Past year†									
No	520	5,235	1.00	509	5,051	1.00	528	5,176	1.00
Yes	16	113	2.18 (1.25-3.80)	27	297	0.98 (0.63–1.54)	8	172	0.67 (0.33-1.40)
Part 1-5 yr									
No	514	5,186	1.00	485	4,955	1.00	522	5,102	1.00
Yes	22	162	1.84 (1.15-2.94)	51	393	1.43 (1.01-2.05)	14	246	0.71 (0.41-1.25)
Career									
No	509	5,148	1.00	441	4,731	1.00	516	5,022	1.00
Yes	27	200	1.59 (1.04-2.45)	95	617	1.59 (1.18-2.14)	20	326	0.69 (0.43-1.11)

*Adjusted for the effects of work (in work or out of work), social class, location in the United States (East or West), and exposure to solvents and sunlight.
†Past year = employment at calendar year of death; past 1-5 yr = ever employed 1-5 years before death; career = longest held job throughout career.

death, with an increased risk for men aged 35 to 49 years (OR, 2.19; 95% CI, 1.12-4.28). Analyses for other exposure windows generally yielded ORs close to or less than 1.00 (data not shown).

DISCUSSION

The results of this study provide support for the hypothesis that occupational exposure to EMFs is associated with an increased risk of suicide. Men employed as electricians, and to a lesser extent as line workers, seemed to be at increased risk, broadly consistent with indications of increased incidences of diagnosed depression and several depressive symptoms in electricians.[37] Power plant operators, however, did not show increased risks. This discrepancy in results could be partially explained by a variation in exposure to levels or patterns of EMFs between those groups. Assessment of exposure to magnetic fields by Kromhout and colleagues showed highest exposures for electricians (1.11 μT) compared with line workers (0.65 μT) and power plant operators (0.79 μT).[28] Also, the inconsistent findings across these jobs could be explained by varying exposure levels of other components of EMFs, which were not captured by our technique of assessing exposure. For example, Armstrong and associates reported high potential exposure to pulsed EMFs for line workers, moderate exposure to pulsed EMFs for electricians, and low exposure to pulsed EMFs for power plant operators.[38]

As expected, men currently working had a substantially decreased risk of suicide, which reflected the healthy worker effect.[36] The increased OR for being out of work indicates that active workers are more physically and mentally fit than those who left the industry and, therefore, tend to be at lower risk of committing suicide. Exposure to sunlight at the workplace seemed to have a small positive association with the risk of suicide, inconsistent with previously reported findings of an association of suicide with decreased exposure to sunlight.[32-34] Nevertheless, a

Table 3 *Adjusted* conditional logistic regression odds ratios (ORs) (95% confidence intervals [CIs]) for suicide relative to cumulative exposure to magnetic fields*

Exposure level, μT-yr	Cases, No.	Controls, No.	OR (95% CI)
Recent exposure			
0	294	2,353	1.00
>0-0.029	58	796	1.19 (0.75-1.89)
0.03-0.049	62	811	1.41 (0.85-2.34)
0.05-0.11	62	719	1.63 (0.97-2.71)
>0.12	60	669	1.70 (1.00-2.90)
Past 1-5 yr			
0	222	1,857	1.00
>0-0.10	75	624	1.25 (0.90-1.75)
0.11-0.19	95	1,338	1.12 (0.76-1.64)
0.20-0.35	73	792	1.45 (0.97-2.17)
>0.36	71	737	1.53 (1.01-2.31)
Past 5-10 yr			
0	202	1,688	1.00
>0-0.13	101	1,254	0.71 (0.53-0.95)
0.14-0.24	89	861	1.01 (0.74-1.39)
0.25-0.43	42	450	0.91 (0.62-1.33)
>0.44	102	1,095	1.00 (0.73-1.38)
Past 10-20 yr			
0	157	1,683	1.00
>0-0.13	93	772	1.09 (0.78-1.53)
0.14-0.32	98	909	1.14 (0.82-1.61)
0.33-0.69	94	943	1.09 (0.77-1.55)
>0.70	94	1,041	1.05 (0.73-1.53)
Past >20 yr			
0	314	3,044	1.00
>0-0.18	57	522	0.91 (0.59-1.41)
0.19-0.43	54	460	0.96 (0.60-1.53)
0.44-1.04	55	588	0.81 (0.50-1.30)
>1.05	56	734	0.72 (0.42-1.21)
Total exposure			
<0.25	133	1,181	1.00
0.25-0.64	135	1,212	1.26 (0.96-1.67)
0.65-1.54	134	1,474	1.13 (0.83-1.53)
1.55-3.00	79	888	1.20 (0.83-1.71)
>3.01	55	593	1.33 (0.89-2.01)

*Adjusted for the effects of work (in work or out of work), social class, location in the United States (East or West), and exposure to solvents and sunlight.

Table 4 *Adjusted* conditional logistic regression odds ratios (ORs) (95% confidence intervals [CIs]) for suicide relative to workers' cumulative exposure to magnetic fields, by age groups*

Exposure level, percentile	Age <35 yr Cases	Controls No.	OR (95% CI)	Age 35-49 yr Cases	Controls No.	OR (95% CI)	Age ≥50 yr Cases	Controls No.	OR (95% CI)
Recent exposure†									
0	38	341	1.00	86	527	1.00	170	1,485	1.00
>0-49	39	431	2.12 (0.98-4.59)	41	651	2.40 (1.04-5.55)	46	574	0.67 (0.32-1.42)
≥50	39	398	2.39 (1.00-5.69)	43	517	3.62 (1.41-9.29)	34	424	0.27 (0.32-1.62)
Past 1-5 yr‡									
0	24	210	1.00	73	457	1.00	125	1,190	1.00
>0-49	49	544	1.20 (0.63-2.27)	48	674	1.48 (0.84-2.62)	75	764	1.35 (0.86-2.11)
≥50	43	416	1.50 (0.72-3.10)	49	564	2.19 (1.12-4.28)	50	529	1.48 (0.88-2.49)

*Adjusted for the effects of work (in work or out of work), social class, location in the United States (East or West), and exposure to solvents and sunlight.
†50 Percentile 0.07, 0.08, and 0.05 μT-years for age <35, 35-49, and ≥50 years, respectively.
‡50 Percentile 0.20, 0.21, and 0.22 μT-years for age <35, 35-49, and ≥50 years, respectively.

mechanism of action of light on suicide could involve inhibition of melatonin synthesis because light has an acute suppressing effect of melatonin synthesis in humans.[39] The higher risk of suicide for workers living in the western United States is consistent with historical trends.[3,4]

An association of suicide with exposure to EMFs was first suggested by Reichmanis and co-workers.[40] Results indicated that the calculated strengths of EMFs at the residences of suicide victims differed from those at the residences of controls. Perry and associates measured magnetic fields and found that the strength of magnetic fields was greater at addresses of those who committed suicide than at addresses of controls.[41] However, other studies did not confirm the findings of these 2 initial reports. In a study of mortality of people residing in the vicinity of electricity transmission facilities, McDowall observed 8,000 people and found a standardized mortality ratio of 75 for 8 cases.[42] Baris and Armstrong found no increased rate of suicide in men with occupations likely to have resulted in exposure to electric and magnetic fields.[43] In another study, Baris and colleagues[44] found some evidence of an association with cumulative exposure to the geometric mean of electric fields among electric utility workers but considered the evidence for a causal association to be weak. Kelsh and Sahl found a consistent association of suicide with nonoffice occupations in the electric utility workforce.[45] Johansen and Olsen found, on the basis of 133 observed cases, no indication of excess mortality from suicide as a result of exposure to 50-Hz magnetic fields.[46] Nonetheless, all studies on suicide and EMFs have been limited in the quality of assessment of exposure, sample size, or information on confounding factors.

Wilson postulated that long-term exposure to EMFs may affect pineal function by interfering with tonic aspects of neuronal input to the pineal gland from the central nervous system and that this disruption of normal circadian rhythmicity, particularly in the synthesis of melatonin, may in turn contribute to depressive symptoms.[5] In the present study, an association was found with cumulative exposure in the calendar year before the year of death, which can be considered to be long-term exposure rather than recent exposure in the context of Wilson's hypothesized mechanism.[5] High exposure to EMFs may cause depression, which, as an intermediate variable, may lead to problems at work—for example, calling in sick more often or changing jobs—or even stopping work (and thereby stopping exposure) before suicide occurs. Consequently, lower exposure levels in the intervals shortly before death may not reflect any causal effect of exposure.

Exposure to EMFs may alter melatonin secretion within days or weeks, supported by studies of users of electric blankets[6] and railway and electric utility workers.[7,8] Consequently, depressive symptoms and related problems may develop in the months between recent exposure and suicide. Although recent exposure showed notable increases in risk, if it had been possible to ascertain exposures closer to time of death, such exposures may have shown a stronger association. Studies capable of resolving exposure and its effects over weeks or months would be informative.

An association between recent exposure to EMFs and suicide was found in younger but not older workers, suggesting that younger people may be more vulnerable to the effects of exposure to EMFs. A difference in the nature of depression and suicide between age groups may account for this increased vulnerability. Depression can be subdivided into 2 categories: minor and major depression. The most important risk factor for minor depression, which is common and important in later life, seems to be medical illness. Major depression was found not to be associated with physical health[47] and is more common among younger age groups.[21] The change in the nature of depression with age suggests that people at a younger age may be more vulnerable to the effects of exposure to EMFs, resulting in depressive disorders and suicide.

The results of this study must be interpreted with rec-

ognition of the limitations of the use of job titles to estimate exposure to EMFs over decades of work experience. Job titles explain only a small proportion of variability in exposure, as diversity across multiple work environments, electric utility companies, job tasks, and responsibilities contribute to the total variation in exposure to EMFs.[48] Also, the component of EMFs that may be relevant to biologic effects remains uncertain,[49,50] and the current techniques for assessing exposure to EMFs, which focus on time-weighted average magnetic fields, can be considered to be only crude measures. Nevertheless, the assessment of exposure to EMFs used in our study is more thorough than in most previous epidemiologic studies on this topic.

An advantage over previous studies is the relatively large sample size, which made it possible to examine individual jobs and stratify by age. Furthermore, our ability to reproduce well-known associations with work status and location in the United States was encouraging. Finally, it is unlikely that misclassification of cases has occurred. Moyer and co-workers examined the agreement between death certificates for causes of death related to injury and an independent medical review of medical and legal records for deaths occurring among US Army Vietnam war veterans.[51] Sensitivity for broad and specific suicide categories was more than 90%, whereas specificity was 100%. This indicates that the use of death certificates is a valid method of classifying suicides. On the other hand, we were unable to isolate suicide deaths mediated by depression from other suicides, including those related to chronic disease, for which the exposure under study would not be relevant.

An important limitation was the inability to fully examine and control for confounding. Information on several important risk factors for suicide was not available, such as history of mental and addictive disorders and disrupted family environment. Nevertheless, some evidence exists that electrical workers and nonelectrical workers are generally similar in sociodemographic and related attributes and tend to drink less alcohol than other workers.[37] Also, a study by Baris and colleagues showed similar exposure among alcohol users compared with nonusers.[44] The same study, however, showed higher exposure among single workers and workers with mental disorders, so that the lack of adjustment for confounding by marital status and mental disorders could have led to the overestimation of an association. Whether these results are applicable to the present study population is unclear. Nevertheless, it seems unlikely that confounding by unmeasured factors or imprecise measurement on the others has occurred in a sufficient degree to create or mask sizable associations.

CONCLUSIONS

The results of this study provide evidence for an association between cumulative exposure of extremely low–frequency EMFs and suicide, especially among younger workers. We hypothesize that an increased vulnerability at younger ages may be based on a change in the nature of depression with age, with suicide more closely linked to depression among younger workers and physical impairments among older workers. Future research on the effects of exposure to EMFs on suicide and depression is warranted to examine more closely the temporal pattern of exposure, depression, and suicide.

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COMMENTARY

Magnetic field exposure may not have a directly causal relationship to suicide

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Work-related suicide? Suicide at work? Work-induced suicide? The definitional issues tying work life to suicide, which by its nature has a multicausal pathway, are complex. These complexities, perhaps, explain why so little research has been conducted on the association between work factors and suicide.

Although the incidence of violent injuries in general has decreased dramatically since 1994, overall suicide rates have decreased only slightly from 1987 through 1997. Among men older than 19 years, suicides have decreased about 8% during this period. According to the Census of Fatal Occupational Injuries (CFOI) conducted by the Bureau of Labor Statistics, the number of suicides identified as being work-related has been stable since 1992.[1] However, the coding issues leading to classifying a suicide as work-related are problematic and inconsistent throughout the country, and the number of events that have a work-related component are probably underestimated. Of more than 1,500 work-related suicides identified by CFOI, less than 1% were in the electric utility industry.

van Wijngaarden and colleagues find an increased risk for suicide among electric utility workers who have been exposed to magnetic fields. They offer a biologic pathway for this relationship, citing the effects of electromagnetic

radiation on disturbances of melatonin regulation. Decreased melatonin production has been linked to depression, which in turn is a risk factor for suicide.

Magnetic field exposure is unlikely to be either a necessary or sufficient cause of depression or suicide, and its role relative to other predictive factors is likely to be small. However, certain persons may have increased vulnerability to this type of exposure, or interactive effects with other predictors of suicide may define particularly vulnerable times. This is a well-conducted study using available information, and the use of defined working cohorts is a rich source for etiologic research. However, the inability in this study to control for the main known predictors of suicide, such as drug use, mental illness, and family and social stresses, and especially the inability to measure depression and its onset severely limit the ability to define the role of electromagnetic exposure in the causal pathway of suicide.

The study found that the strongest risk for suicide was among the most recent exposures, suggesting either a relatively short latency period or a strong survival effect. Such a survival effect, in which those most vulnerable to exposure commit suicide early and those less vulnerable continue to accumulate exposure, is supported by the authors' theory that electromagnetic radiation has a stronger relationship with types of depression found among younger people. The relatively short latency—in contrast to the relation between depression and suicide, which is a complex path with a long latency—suggests the possibility that magnetic fields operate as a prognostic factor rather than a risk factor to exacerbate the effects of existing depression or other risk factors for suicide, possibly leading to increased suicidal ideation. Most cases of depression do not lead to suicide, and other mental illnesses are much more predictive of suicidal behavior. If exposure to electromagnetic fields does increase the risk for depression or worsen depressive symptoms, treatment and prevention should focus on the depressive symptoms themselves.

What implications do these findings have for occupational medicine physicians? Although they certainly open the door for future research, the practical implication is that workers exposed to electromagnetic fields should be aware of the signs and symptoms of depression, and their physicians should ask about these symptoms during history taking and clinical examination. Primary care physicians should be aware of these symptoms in any of their working patients. Future research will hopefully elucidate the biologic pathway of this relationship, leading to more sophisticated prevention and treatment measures.

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Physical activity and peptic ulcers

Does physical activity reduce the risk of developing peptic ulcers?

ABSTRACT **Background** Although *Helicobacter pylori* has been identified as a major cause of chronic gastritis, not all infected patients develop ulcers, suggesting that other factors such as lifestyle may be critical to the development of ulcer disease. **Objective** To investigate the role physical activity may play in the incidence of peptic ulcer disease. **Methods** The participants were men (n = 8,529) and women (n = 2,884) who attended the Cooper Institute for Aerobics Research, Dallas, Texas, between 1970 and 1990. The presence of gastric or duodenal ulcer disease diagnosed by a physician was determined from a mail survey in 1990. Participants were classified into 3 physical activity groups according to information provided at the baseline clinic visit (before 1990): active, those who walked or ran 10 miles or more a week; moderately active, those who walked or ran less than 10 miles a week or did another regular activity; and the referent group consisting of those who reported no regular physical activity. **Results** With the use of gender-specific proportional hazards regression models that could be adjusted for age, smoking, alcohol use, body mass index, and self-reported tension, active men had a significantly reduced risk for duodenal ulcers (relative hazard [95% confidence interval] for the active group, 0.38 [0.15-0.94], and 0.54 [0.30-0.96] for the moderately active group). No association was found between physical activity and gastric ulcers for men or for either type of ulcer for women. **Conclusion** Physical activity may provide a nonpharmacologic method of reducing the incidence of duodenal ulcers among men.

Peptic ulcer disease is one of the most common disorders affecting the digestive system. In 1989, 10% of adult residents of the United States (an estimated 18 million people) reported ever having had ulcer disease diagnosed by a physician, and about a third of those reported having an ulcer within the preceding year.[1] Since Marshall and Warren suggested that *Helicobacter pylori* may play a role in gastritis-associated diseases,[2] *H pylori* infection has been confirmed as the major cause of chronic gastritis throughout the world. Exposure to this organism occurs in childhood and is common in many areas of the world. In the United States, the prevalence of *H pylori* infection is

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higher among blacks and among groups with low education and low income levels, indicating that socioeconomic conditions may affect exposure.[3]

Although *H pylori* infection is common worldwide, ulcers develop in only a minority of infected patients.[4,5] Various host factors or cofactors other than *H pylori* are probably critical to the development of peptic ulcer disease in infected people.[5-9] Besides *H pylori*, smoking, alcohol consumption, and psychological stress have been identified as risk factors (or cofactors) for peptic ulcer disease,[9-11] suggesting that, even if *H pylori* is causal for some types of peptic ulcer disease, other factors may play an important contributing role.[6-8]

Although physical activity has been shown to provide numerous benefits for psychological and physical health,[12] studies of the effect of physical activity on the development of peptic ulcer disease, controlling for psychological tension, have not been reported. Physical activity could possibly affect peptic ulcer disease through several biologic mechanisms, including enhancing the immune system's ability to neutralize the effects of *H pylori*, reducing excess acid secretion, and improving a person's ability to cope with stressful situations. The purpose of this study is to explore the relation between physical activity and peptic ulcer disease among men and women, controlling for age, smoking habits, alcohol use, body mass index (BMI), and psychological tension.

Summary points

- Physical activity has numerous health benefits and may also represent a cost-effective approach to the prevention of peptic ulcers
- At the levels observed in this study among the moderately active group (walking or jogging <10 miles a week), possible adverse effects—for example, injuries—are minimized
- In the general population, only about a third of adults undertake this much physical activity
- Strategies to promote safe walking, jogging, and cycling may benefit many aspects of health in addition to the cardiovascular and musculoskeletal systems

PARTICIPANTS AND METHODS

Data sources

Study subjects were selected from those who received a medical examination at the Cooper Institute for Aerobics Research, Dallas, Texas, between 1970 and 1990. All subjects completed a detailed questionnaire and underwent a clinical evaluation, including a physical examination by the physician.

Information obtained included personal characteristics (age and sex), medical status, clinical measures, medical history, lifestyle habits (tobacco use, alcohol use, and physical activity), and a measure of psychological tension (that is, stress). Between 1970 and 1990, 36,605 people (28,315 men and 8,290 women) were examined at least once. They came from all 50 states, and were predominantly male (80%) and white (97%). Participants were well educated and from middle to upper socioeconomic strata; more than 75% had graduated from college.

A mail-back survey completed in 1990 asked for detailed self-reported information on illnesses and conditions diagnosed by a physician. The questionnaires were sent to everyone who had ever attended the Cooper clinic. The final response rate after multiple mailings was 63% (not including questionnaires with incorrect addresses).

Participants were included in this analysis if they were older than 20 years at the first clinic visit, had a baseline examination between 1970 and 1990, and responded to a mailed questionnaire in 1990 (at least 6 months after their clinic examination). The 231 who had an ulcer diagnosis at their first clinic visit were excluded. The final sample size was 11,413 (8,529 men and 2,884 women).

Outcome variables

Although ulcers of the stomach (gastric ulcers) or of the upper intestine (duodenal ulcers) are grouped as peptic ulcers, they are distinct diseases with important pathologic differences. Therefore, despite the small number of new cases, peptic ulcerations of the stomach and duodenum were distinguished in this study.

The presence of diagnosed ulcer disease was reported by participants in the follow-up survey in 1990. Although the accuracy of self-reported peptic ulcer disease diagnosed by a physician is not known, this cohort has shown high sensitivity and specificity for diagnosed hypertension (98% and 99%, respectively).[13] High sensitivity and specificity for hypertension (82% and 98%, respectively) have also been reported in other data sets of well-educated adults.[14] A national survey in the United States found that about 75% of those who self-reported ulcer disease had their diagnosis confirmed by a physician.[1] Because of this evidence, we are unlikely to have large misclassification errors by using self-report data on ulcer disease to classify these well-educated people as to their disease status.

Independent variables

Physical activity was assessed at baseline and determined by self-reported regular walking and jogging and other activities. Participants who did not participate in regular walking or jogging or any other leisure time physical activity were the referent group; those who walked or jogged up to 10 miles a week or reported regular participation in another activity were considered moderately active; and

those who walked or jogged more than 10 miles a week were considered active.

In this analysis, current smokers were compared with those who had never smoked or who had quit smoking by the time of the baseline examination, which was before the ulcer diagnosis. Information on alcohol use was obtained at the baseline clinic examination and the data converted to ethanol consumption as follows: 1.1 g for 1 oz of beer, 2.7 g for 1 oz of wine, and 15.1 g for 1 oz of spirits.[15] Ethanol consumption was categorized into 4 levels: none (reference level); 0.1 to 13.2 g a day (equivalent to 1 drink a day); 13.21 to 26.4 g a day (equivalent to 2 drinks a day); and 26.41 g or more a day (equivalent to >2 drinks a day).

Psychological stress has been shown to have a strong effect on the gastrointestinal system, and there is some evidence that it may cause peptic ulcers.[10] To assess psychological tension as a marker for stress, we used the question (from the baseline record), "How would you classify yourself on the following tension and anxiety scale?" The 5 possible choices were no tension or very relaxed; slight tension; moderate tension; high tension; and very tense or highly strung. We identified people with high tension as those who reported either having high levels of tension or that they were very tense or highly strung.

Weight and height were measured on a standard physician's scale at the first (baseline) clinic visit. The BMI was calculated as weight (kg) divided by height^2 (m^2). The BMI was divided into 3 levels: lowest 25% (cutoff point, 23.5), highest 25% (cutoff point, 27.4), and the middle group, which served as the reference. Age and BMI were used as control variables. Other potential confounders such as race or ethnicity, socioeconomic status, and educational status were not included because most of the participants were white and well educated.

Statistical analysis

Analyses were conducted using commercial statistical software (Statistical Analysis System, version 6; SAS Institute, Inc, Cary, NC). χ^2 and trend tests were used to summarize categorical variables. Instantaneous relative risk (RR) was derived from the Cox proportional hazards model using the time of observation. Considering the differences between men and women in lifestyle, occupation, and other unmeasured factors that are difficult to control adequately in the models, we developed gender-specific Cox regression models. Because of missing values for the psychological tension variable (n = 645), Cox models were developed first for the whole group without including psychological tension as an independent variable. Subsequently, Cox models were developed for the subset of subjects who had been asked the psychological tension question. We included all variables in building each model to evaluate the effect of each variable while controlling for all others.

RESULTS

Descriptive analysis

After the omission of participants who had a diagnosis of peptic ulcer disease before the baseline visit and those who had missing information on physical activity patterns, ulcer diagnoses, smoking habits, alcohol use, weight, or height, 11,413 people (8,529 men [74.7%] and 2,884 women [25.3%]) were available for study. The mean age was 45 (range, 20-87) years. Between the time of the baseline examination and the mail-back survey, new duodenal ulcers developed in 61 men and 13 women and new gastric ulcers developed in 116 men and 42 women.

Tables 1 and 2 show a possible protective effect of both moderate and high levels of physical activity on the development of duodenal or gastric ulcers among men, and the χ^2 trend test suggests a dose-response trend for both duodenal ulcer ($P = 0.001$) and gastric ulcer ($P = 0.01$). Results also show that current smoking and high levels of tension were risk factors for duodenal ulcer (among men) and that high levels of tension were a risk factor for gastric ulcer for both men and women. For men, smoking was associated with an increased risk of gastric ulcers, but light and moderate amounts of alcohol consumption were protective, although the trend test for alcohol consumption was not statistically significant. The results shown in tables 1 and 2 are not adjusted for any of the covariates, nor are they adjusted for the length of observation.

Cox proportional hazards models

The results of the Cox proportional hazards models that include all of the possible risk factors except psychological tension were similar to those models that included psychological tension, which are reported here and shown in table 3. For men, inactivity and the presence of psychological tension were risk factors for duodenal ulcer. Also for men, smoking and psychological tension were positively associated with gastric ulcers; alcohol consumption had a U-shaped relation, with moderate intake inversely associated with the development of gastric ulcer. For women, the only significant finding was that psychological tension was associated with gastric ulcer development ($P < 0.001$).

DISCUSSION

Peptic ulcer disease is a common clinical problem. The lifetime risk of peptic ulcer disease is 5% to 10% in developed countries.[1,16,17] The pathophysiologic characteristics of peptic ulcer are complicated and may involve an

Table 1 *Rate ratios of potential risk factors for self-reported duodenal ulcers, Cooper Institute for Aerobics Research, Dallas, Texas, 1970-1990*

Risk factor	Men (n = 8,529) Cases, No.	Subjects, No.	RR (95% CI)	Women (n = 2,884) Cases, No.	Subjects, No.	RR (95% CI)
Physical activity						
Active	6	2,059	0.23 (0.10-0.55)	3	563	0.82 (0.21-3.28)
Moderately active	20	3,686	0.43 (0.25-0.75)	4	1,395	0.44 (0.13-1.56)
Referent	35	2,784	1.00	6	926	100
	Trend test: $\chi^2 = 16.71$, $P = 0.001$			Trend test: $\chi^2 = 0.29$, $P = 0.59$		
*Psychological tension**						
High	22	1,905	2.28 (1.32-3.92)	2	635	0.74 (0.16-3.42)
Low	31	6,112	1.00	9	2,116	1.00
Smoking						
Yes	52	3,362	1.70 (1.03-2.08)	4	1,043	0.78 (0.24-2.54)
No	29	5,167	1.00	9	1,841	1.00
Ethanol consumption						
Heavy	12	2,059	0.82 (0.40-1.70)	1	325	0.67 (0.08-5.75)
Moderate	8	1,507	0.75 (0.33-1.72)	1	369	0.59 (0.07-5.04)
Light	23	2,421	1.34 (0.73-2.48)	6	1,098	1.19 (0.37-3.90)
None	18	2,542	1.00	5	1,092	1.00
	Trend test: $\chi^2 = 0.81$, $P = 0.37$			Trend test: $\chi^2 = 0.04$, $P = 0.85$		
Age						
>60	5	537	1.30 (0.49-3.41)	1	179	1.31 (0.15-11.13)
40.1 to 60	34	4,927	0.96 (0.56-1.64)	7	1,535	1.07 (0.34-3.35)
20 to 40	22	3,065	1.00	5	1,170	1.00
	Trend test: $\chi^2 = 0.06$, $P = 0.81$			Trend test: $\chi^2 = 0.05$, $P = 0.82$		
Body mass index						
Higher 25%	12	1,923	0.89 (0.46-1.71)	1	618	0.38 (0.05-3.09)
Reference	33	4,684	1.00	7	1,650	1.00
Lower 25%	16	1,922	1.18 (0.65-2.14)	5	616	1.91 (0.61-6.01)

RR = risk ratio; CI = confidence interval
*The number of subjects in this category differs because only a subset of respondents was asked about psychological tension.

overproduction of acid or pepsin, inadequate mucosal defenses, or reflux of bile and pancreatic juice into the stomach.[18] Although *H pylori* is considered causal for peptic ulcer disease, infection is widespread in developed and developing countries, but few people actually develop peptic ulcers.[4,19] The epidemiologic data for peptic ulcer disease do not suggest a single cause but instead multiple etiologic factors, including socioeconomic indicators, psychosocial factors, *H pylori* infection, and cigarette smoking.[9]

Physical activity may be involved in the pathogenesis of peptic ulcer disease through several mechanisms, one of which may involve the immune system. Although epidemiologic studies suggest that regular moderate physical activity is associated with a lower risk of bacterial infections (upper respiratory tract infections),[20] and experimental studies document an alteration in immune status in athletes and nonathletes in response to exercise,[21] the issue is far from resolved. Even when these changes are documented, the immune system is not necessarily enhanced. In fact, overexertion of the physical system can have an overall adverse effect on immune system variables, similar to the proposed effect of stress. Because the experimental studies that show increases or decreases in a myriad of immune variables have not been able to connect these results with clinical illness, this mechanism is hypothetical at this stage.[22]

Another possible mechanism through which physical activity may affect the development of ulcer disease is decreased acid secretion. A few studies report a decrease in basal or meal-stimulated acid secretion with cycling and after exertion, leading to suggestions that exercise may assist in duodenal ulcer healing and maintenance of remission.[23-25] Regular physical activity (walking, gardening, or vigorous physical activity) has been associated with a decreased risk for severe gastrointestinal hemorrhage in older subjects with gastroduodenal ulcer or gastritis (RR = 0.4, 95% confidence interval [CI] = 0.3-0.7).[26] In our study, after confounding variables had been controlled for, physical activity was found to be inversely related to the incidence of duodenal, but not gastric, ulcers for men only. This finding may be consistent with other studies if the effect of reduced acid secretion is more important for the duodenum, but this is difficult to determine because most studies combine duodenal and gastric ulcers. Also,

Table 2 *Rate ratios of potential risk factors for self-reported gastric ulcers, Cooper Institute for Aerobics Research, Dallas, Texas, 1970-1990*

Risk factor	Men (n = 8,529) Cases, No.	Subjects, No.	RR (95% CI)	Women (n = 2,884) Cases, No.	Subjects, No.	RR (95% CI)
Physical activity						
Active	19	2,059	0.51 (0.30-0.87)	6	563	0.55 (0.22-1.37)
Moderately active	47	3,686	0.71 (0.48-1.05)	18	1,395	0.66 (0.35-1.27)
Referent	50	2,784	1.00	18	926	1.00
		Trend test: $\chi^2 = 6.97$, $P = 0.01$			Trend test: $\chi^2 = 2.18$, $P = 0.14$	
*Psychological tension**						
High	36	1,905	1.83 (1.22-2.75)	16	635	2.67 (1.39-5.11)
Low	63	6,112	1.00	20	2,116	1.00
Smoking						
Yes	56	3,362	1.43 (1.01-2.06)	18	1,043	1.32 (0.72-2.43)
No	60	5,167	1.00	24	1,841	1.00
Ethanol consumption						
Heavy	32	2,059	0.86 (0.55-1.34)	6	325	1.26 (0.50-3.19)
Moderate	13	1,507	0.48 (0.26-0.88)	6	369	1.11 (0.44-2.82)
Light	25	2,421	0.57 (0.35-0.93)	14	1,098	0.87 (0.43-1.77)
None	46	2,542	1.00	16	1,092	1.00
		Trend test: $\chi^2 = 0.80$, $P = 0.37$			Trend test: $\chi^2 = 0.24$, $P = 0.63$	
Age						
>60	7	537	1.21 (0.54-2.72)	1	179	0.41 (0.05-3.06)
40.1 to 60	76	4,927	1.43 (0.95-2.15)	25	1,535	1.15 (0.64-2.22)
20 to 40	33	3,065	1.00	16	1,170	1.00
		Trend test: $\chi^2 = 1.84$, $P = 0.18$			Trend test: $\chi^2 = 0.17$, $P = 0.68$	
Body mass index						
Higher 25%	30	1,923	1.18 (0.76-1.82)	4	618	0.38 (0.13-1.08)
Reference	62	4,684	1.00	28	1,650	1.00
Lower 25%	24	1,922	0.94 (0.59-1.51)	10	616	0.96 (0.47-1.96)

RR = risk ratio; CI = confidence interval
*The number of subjects in this category differs because only a subset of respondents was asked about psychological tension.

our study showed a similar effect of physical activity on both gastric and duodenal ulcers when evaluated without adjusting for other potential confounders.

Another possible mechanism by which physical activity can reduce the incidence of duodenal ulcers is through its effect on stress. The role of physical activity in reducing stress has not been clearly defined, probably because of the difficulty of developing a consistent definition of psychological stress. In cross-sectional studies and clinical trials, moderate levels of physical activity have been associated with stress-related emotions such as anxiety.[27,28] Although the data are not totally consistent at this point, some evidence exists that increased physical conditioning or fitness enhances a person's ability to deal with the physiologic response to psychological stress.[29]

A recent update concludes that stress is a major risk factor for peptic ulcer disease regardless of the presence of *H pylori* infection or nonsteroidal anti-inflammatory drug use.[30] The relation between stress and peptic ulcer disease has been well established.[10,30] In a longitudinal study of adults in the United States,[31] after adjustment for age, sex, education, smoking status, and regular aspirin use, ulcers were 1.8 (95% CI = 1.3-2.5) times more likely to develop in those who perceived themselves as stressed than in those who did not. A graded relation between the perceived amount of stress and incidence of peptic ulcers was also shown. The results of our study, using self-perceived tension as a marker for stress, support this viewpoint.

Not all studies have found a protective effect of physical activity on the development of ulcers. Katschinski and coauthors[32] found physical activity at work to be positively associated with duodenal ulcers. After the values had been adjusted for age, sex, smoking, and social class, the participants who reported high levels of physical activity at work had a higher risk of duodenal ulcer than those who reported sedentary activity at work (RR = 3.6, 95% CI = 1.3-7.8), but moderate activity at work was not associated with duodenal ulcer (RR = 1.3, 95% CI = 0.6-3.0). Although the data were controlled for social class, people who have jobs with high physical demands (that is, laborers) may also have high levels of stress or other lifestyle exposures—for example, *H pylori* infection—that were not considered in the analysis. In part, the inconsistencies found among these studies may reflect differences

Table 3 *Risk ratio of all potential risk factors using Cox proportional hazards model, Cooper Institute for Aerobics Research, Dallas, Texas, 1970-1990*

Risk factor	Men: Duodenal ulcer HR (95% CI)	Men: Gastric ulcer HR (95% CI)	Women: Duodenal ulcer HR (95% CI)	Women: Gastric ulcer HR (95% CI)
Moderately active	0.54 (0.30-0.96)	1.08 (0.51-2.27)	0.62 (0.15-2.53)	1.08 (0.69-1.69)
Active	0.38 (0.15-0.94)	1.01 (0.56-1.82)	1.47 (0.32-6.83)	1.19 (0.44-3.25)
High tension	1.97 (1.14-3.43)	1.57 (1.04-2.38)	0.66 (0.14-3.10)	2.52 (1.30-4.89)
Smoking	1.91 (1.09-3.35)	1.71 (1.13-2.58)	0.61 (0.15-2.45)	1.14 (0.57-2.28)
Ethanol (light)	1.90 (0.90-4.02)	0.65 (0.38-1.11)	1.93 (0.47-7.88)	1.11 (0.48-2.53)
Ethanol (moderate)	0.80 (0.31-2.05)	0.43 (0.22-0.83)	0.80 (0.08-7.88)	1.15 (0.41-3.23)
Ethanol (heavy)	0.77 (0.33-1.80)	0.72 (0.43-1.21)	2.56 (0.39-16.92)	1.28 (0.44-3.70)
Age (40-60 yr)	1.07 (0.59-1.94)	1.24 (0.80-1.93)	0.63 (0.18-2.24)	1.13 (0.57-2.24)
Age (>60.1 yr)	1.95 (0.72-5.33)	1.26 (0.52-3.05)	1.16 (0.13-10.22)	0.62 (0.08-4.73)
BMI (upper 25%)	1.13 (0.60-2.14)	1.04 (0.63-1.74)	2.00 (0.55-7.35)	1.25 (0.57-2.74)
BMI (lower 25%)	0.64 (0.29-1.40)	1.04 (0.64-1.70)	0.39 (0.05-3.28)	0.41 (0.14-1.21)

HR = hazard ratio; CI = confidence interval; BMI = body mass index

in the measurement of physical activity as well as other factors, such as the level of stress.

Two related behaviors, cigarette smoking and alcohol consumption, have been variously implicated as risk factors for peptic ulcer disease. As in other studies,[1,11,33,34] we found both gastric and duodenal ulcer disease to be strongly associated with cigarette smoking, even after controlling for other possible risk factors. Excessive alcohol consumption causes damage to the stomach or duodenum by impairing the integrity of the mucosal barrier.[35] In our study, however, we found a protective effect of moderate consumption of alcohol (1 or 2 drinks a day) on the development of gastric ulcer in men, even after controlling for tension. This finding suggests that some of the adverse effects of alcohol may be attributed to alcohol-associated behavior, such as smoking. A seroepidemiologic study of smoking and alcohol consumption on serum levels of pepsinogen I, pepsinogen II, or pepsinogen I:II ratio conducted among 13,381 employees using a questionnaire and serum test[36] concluded that current smoking elevated the pepsinogen I level and the I:II ratio and that drinking reduced pepsinogen I and II levels, but the effect was small. As in the current study, other studies found drinking alcohol to be either a protective factor or not associated with peptic ulcer.[37-39] Drinking moderate amounts of alcohol has also been shown to protect against active infection with *H pylori*.[40,41] The possibility exists that alcohol consumption may be related to positive or negative risk factors, depending on the dose and type of drinking.

Weatherall and Shaper found that mean BMIs decreased with increasing levels of physical activity, and peptic ulcer disease was inversely related to BMI in 7,735 middle-aged overweight and obese men in 24 British towns.[42] In the Cooper clinic data, in people of primarily normal weight, we found no evidence of a relation between BMI and peptic ulcer disease.

Sonnenberg and Everhart reported that age was not associated with gastric ulcer development in National Health Interview Survey data but was associated with duodenal ulcer development.[1] We did not find age to be associated with either type of ulcer disease. One explanation for this variation is that peptic ulcer disease is a chronic condition, older populations may have a higher prevalence, and in our study, only new (incident) cases were analyzed. Another explanation is that, if *H pylori* is a causal factor, older people would have a longer window for exposure, and a higher prevalence among older people may reflect an aging-related decline in immune function. However, because the prevalence of *H pylori* is strongly associated with low income, low levels of education, and nonwhite race, and because our study participants were not in these risk groups, it is possible that, for these participants, *H pylori* infection did not play a major role in the development of their peptic ulcer disease. This would also explain the lack of an effect of age on the development of peptic ulcers found in this study.

Our findings for women differed from those for men, and this may reflect a different level of intensity for the reported physical activity between men and women. Our study looked at the type and duration of physical activity

but not intensity. In addition to intensity, the type of physical activity reported may not be representative of all the physical activity that women may do, including housework and child care. The small sample size for women (only 13 cases of duodenal ulcer) was also a disadvantage for this study. Other data sets will need to be analyzed further to clarify the possible relation between physical activity and peptic ulcers in women. If these findings hold, physical activity may prove to be a good candidate for nonpharmacologic intervention to prevent the development of duodenal ulcers among men.

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COMMENTARY

Can we make any recommendations about physical activity and peptic ulcer disease?

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Acid peptic disease is a common disorder that accounts for between 4 and 5 million new or recurrent cases per year in the United States alone.[1] The direct and indirect costs are substantial and are estimated at $12 to $15 billion annually.[2]

In the past 3 decades, our understanding of the causation and treatment of peptic ulcer disease has changed dramatically. The proven association between *Helicobacter pylori* and gastroduodenal ulceration is perhaps the most significant finding,[3] and some researchers now consider peptic ulcer disease to be infectious. The other major causal relationship is between the development of mucosal damage and the ingestion of nonsteroidal anti-inflammatory agents.[4]

Additional risk factors for peptic ulceration can be classified into those that are well founded, such as smoking and chronic obstructive pulmonary disease; those that are possible risks, such as high stress levels[5]; and those of questionable importance, such as genetics, ingestion of alcohol, cirrhosis, and rheumatoid arthritis. Although this last group has previously been considered to have a definite association with ulcer disease, the data were largely obtained in the era when *H pylori* status was not evaluated. Certain chronic disease states may be associated with either different rates of *H pylori* infection or an alteration of the effect on mucosal changes caused by this bacterium.

Cheng and colleagues present data suggesting that physical activity may provide a nonpharmacologic method of reducing the incidence of duodenal ulcers in men. They note that despite the large number of people worldwide who harbor *H pylori*, ulcer disease develops in only a small percentage, and they suggest that some additional lifestyle factors may be involved.

Some 36,000 men and women were evaluated at the Cooper Clinic in Dallas from 1970 through 1990. Baseline information was obtained, including degree of physical activity, smoking habits, alcohol use, self-reported stress levels, age, and body mass index. A questionnaire was then sent out in 1990 to all subjects, except those who had reported a history of peptic ulcer at the time of their initial visit. The respondents, a total of 63% of those mailed a questionnaire, were asked if they had been diagnosed by a physician as having had an ulcer at any time since their baseline evaluation. After those with "incomplete data" were excluded, only 31% of the total group was included.

The results implied that physical activity provided a protective effect for duodenal ulcer in men only. No significant effect was seen for men with gastric ulcers or for women with either gastric or duodenal ulcer disease. Smoking and high levels of stress were risk factors for duodenal ulcers among men, and high levels of stress were a risk factor for gastric ulcer for both men and women. For men, smoking was also associated with an increased risk of gastric ulcer. But before we can suggest to our male patients that they can "run away" from ulcer disease, more data are needed.

Many questions in this study remain unanswered. How was the diagnosis of ulcer made? What about the role of *H pylori* and nonsteroidal anti-inflammatory drugs? To a great extent, the epidemiologic features of peptic ulcer disease have, over the past several decades, paralleled those of *H pylori*. During this period, the prevalence of *H pylori* infection in developed countries has been rapidly declining, and along with this, we have also seen a decrease in the incidence of peptic disease. The patients seen at the Cooper Clinic were predominantly men, white, well educated, and of high socioeconomic status. This group would be expected to have a low rate of *H pylori* infection, although they would not be totally free of the infection. With no data presented on *H pylori* status or the use of nonsteroidal anti-inflammatory drugs, the results are subject to alternative explanations. The baseline data recorded levels of physical activity, as did the 1990 questionnaire. Did all these subjects maintain the same level of activity over the entire 19.5 years? If not, how long is exercise needed to be protective? Were the men in the "activity" group smokers? Did they use more or fewer nonsteroidal anti-inflammatory drugs than the reference group?

Possible mechanisms whereby exercise may reduce ulcer rates are offered, including effects on the immune system and reducing or better coping with stress. Several studies have examined these factors and have been either inconclusive or yielded contrary results. Exercise has been demonstrated to reduce acid secretion, but the effect is modest and short-lived. It is unlikely to have a beneficial effect on a process where healing rates are standardly measured in time scales of 4 to 8 weeks.

So what advice can we give our patients who are anxious to avoid ulcer disease? Physical exercise, in moderation, has been shown to have beneficial effects and should be encouraged, but it benefits the cardiopulmonary and musculoskeletal systems more than the gastrointestinal tract. What can be said with confidence is that a recom-

mendation to stop smoking and avoid using nonsteroidal anti-inflammatory drugs will go a long way.

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Are adolescents being screened for sexually transmitted diseases?

A study of low-income African American adolescents in San Francisco, California

ABSTRACT **Objectives** To determine the proportion of sexually experienced African American adolescents who report having been screened for sexually transmitted diseases and to determine the proportion who report having been screened for these diseases among adolescents who have had a preventive primary health care visit in the past 2 years. **Methods** A telephone survey of a population-based sample of African American adolescents aged 12 to 17 years residing in a low-income neighborhood in San Francisco with a high prevalence of sexually transmitted diseases. **Results** Of the 302 adolescents surveyed, 118 (39.1%) reported a history of sexual intercourse. Of these, 17 (26.2%) of 65 males and 31 (58.5%) of 53 females had been screened for a sexually transmitted disease in the previous 12 months. Twenty (30.8%) of the males and 32 (60.4%) of the females had been screened for a sexually transmitted disease in the previous 24 months. Of the 93 participants who had had a preventive primary care visit since their first episode of sexual intercourse, 14 (26.4%) of the 53 males and 24 (60.0%) of the 40 females had been screened for a sexually transmitted disease in the previous 24 months. **Conclusions** Sexually experienced African American adolescents in San Francisco are being screened for sexually transmitted diseases at rates well below those recommended by current clinical guidelines. A low rate of screening was found even in adolescents who had been seen for a preventive primary care visit since they had first had sex. This suggests that the preventive primary care visit is not being used to its full potential as an opportunity to screen and treat adolescents for sexually transmitted diseases. Capitalizing on this opportunity to screen may increase the number of cases of sexually transmitted diseases diagnosed and, thus, decrease rates of these diseases in this population.

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INTRODUCTION

A cornerstone of prevention and control of sexually transmitted diseases (STDs) is the early diagnosis and treatment of those caused by bacteria. Researchers have shown that testing people for STDs, even in the absence of symptoms, can prevent adverse health outcomes.[1] Accordingly, most current practice guidelines recommend that clinicians test adolescents who have had sexual intercourse for STDs at least annually as part of a primary preventive health visit—that is, during a routine periodic history and physical examination.[2-4] This testing in the absence of symptoms is commonly known as screening. A recent Institute of Medicine report suggests that the integration of STD screening into primary care visits would increase the number of adolescents who are screened for STDs and, thus, would increase the number of adolescents diagnosed as having and being treated for STDs.[5]

Few data are available on how many American adolescents who have had sexual intercourse are screened for STDs. A 1988 US survey showed that 46% of sexually experienced 15- to 19-year-old African American women and 34% of all sexually experienced 15- to 19-year-old women had been tested for STDs in the 12 months before the survey.[6] The researchers found that women were more likely to have been tested for STDs if they had had any of the following: a family planning visit in the 12 months before the survey, a higher number of sexual partners, a recent pregnancy, or a history of an STD. However, because this study did not differentiate between times when women were tested for an STD because of symptoms and times when they were screened in the absence of symptoms, it is difficult to assess the role of primary care in the secondary prevention of STDs. The study also did not include men.

Another study that examined STD screening practices for adolescents reported on laboratory tests done on patients who were enrolled in 7 health maintenance organizations (HMOs) in Massachusetts in 1992.[7] The investigators estimated that 21% of the 15- to 19-year-old sexually experienced women enrolled in the HMOs were tested for STDs. Interestingly, they arrived at this estimate without knowing how many of the adolescents enrolled in the HMOs had a history of sexual intercourse—that is, the number of women who should have been screened. Rather, they had to use data from another study of high school students from Massachusetts to infer the proportion of female adolescents enrolled in the HMOs likely to have a history of sexual intercourse. This method calls into question the reliability of their estimate, and, like the previous study, this one did not differentiate between whether women had symptomatic testing or asymptomatic screening, did not determine the number of adolescent women who had received preventive primary care, and did not include adolescent men.

The limitations of these 2 studies demonstrate how difficult it is to assess whether adolescents are being appropriately screened for STDs. To answer this question properly requires that a community-based sample of adolescents answer detailed questions about their sexual histories to determine which adolescents are sexually experienced, which have had a preventive primary care visit, and which had STD symptoms at the time of the visit.

The objective of this population-based study of African American adolescents was to determine the proportion of sexually experienced African American adolescents who report having been screened for STDs. In addition, we wanted to determine the proportion of sexually experienced adolescents who had been screened for STDs among those adolescents who had attended a primary preventive health visit in the past 2 years. We focused on African American adolescents because the burden of disease is highest in this population. For example, the 1997 reported rate of chlamydia in American adolescents aged 15 to 19 years was 1,126 per 100,000. The reported rate in African American men was more than 12 times and in African American women was more than 6 times the corresponding rates in age-matched white adolescents.[8]

METHODS

This analysis was part of a larger study that examined health-seeking behavior by African American adolescents and was used to inform the development of a community-based intervention to reduce the prevalence of STDs in these youths. Target participants were African American adolescents between the ages of 12 and 17 years who lived in a predominantly low-income, African American neighborhood in San Francisco. The prevalence of reportable STDs in the neighborhood is the highest in the city (San Francisco Department of Public Health, unpublished data, 1999).

Between November 1996 and March 1997, we contacted a sample of households using a list-assisted random-digit set of telephone numbers from 3 different prefixes. More than 98% of households in the neighborhood are estimated to have a telephone service, and 65% of these households are served by the 3 telephone prefixes we used. Potential participants were contacted in the evenings and on weekends. If more than 1 adolescent lived in a household, each was considered eligible to participate. Only adolescents who were identified by their parent or guardian as being African American were enrolled in the study. Verbal informed consent was obtained from both the parent and the adolescent. After the 30-minute telephone interview, adolescents were mailed a check for $10. The study was conducted with approval of the institutional review board.

In all, we contacted 285 households in which 394 eligible adolescents lived. Participation was declined by 13.7% of parents or guardians. A further 9.6% of adolescents either declined consent or were unavailable for interview. There was no difference in age or sex of participants and nonparticipants. Thus, the sample consisted of 302 participants who lived in 224 households and represented 76.6% of eligible participants.

The wording of survey items was based on results of focus groups and pilot tests. Most questions were worded so that adolescents could respond with "yes" or "no" or with a number to maintain the confidentiality of their responses from family members. Whenever possible, participants were interviewed while they were alone in the room. Less than 10% reported that a parent or guardian or other adult was in the same room at any time during the interview.

Basic demographic data (age, sex, and educational level of parents) were collected from each adolescent. Health insurance data were collected from the parent or guardian. Participants were asked a variety of questions about their general health-seeking behavior, including the names of clinics they had attended. We determined whether participants had had a preventive primary care visit by their response to the question: "When was the last time you had a full physical? By a 'full physical,' we mean a visit where they examined your whole body and asked you a lot of questions about your health and things that might affect your health." Participants were then asked whether they had ever had sexual intercourse. This was defined for them as " 'having sex' or 'going all the way,' like when a boy puts his penis in a girl's vagina." Participants who reported a history of sexual intercourse were then asked when they had first had sex and the number of sexual partners they had had in their lifetime. They were then asked if they had ever been checked for an STD when they had symptoms

and when that was. Symptoms were described to them as including times when they had pain or discharge from their penis or vagina that was not urine. Later in the interview, participants were asked if they had ever been checked for an STD when they did not have any symptoms and when that was. In addition, they were asked if they had ever been diagnosed as having, or treated for, any of the following STDs: genital herpes, gonorrhea, chlamydia, pelvic inflammatory disease, and syphilis.

We defined an adolescent as having had a preventive primary care visit if the visit had occurred within the previous 2 years. We determined which participants had a history of sexual intercourse at the time of their primary care visit based on the responses of participants to the questions regarding when they had first had sex and when they last had a preventive primary care visit. To assess the influence of the nonindependence of participants (many of the participants resided in households where another participant resided), we reanalyzed our data including only 1 participant per household. No clinically significant difference between our initial and revised results was found. Thus, we have presented our initial results.

RESULTS

Of the 302 adolescents surveyed, 118 (39.1%) reported at least 1 episode of sexual intercourse. Selected characteristics of these 118 adolescents are shown in table 1. Seventeen of the 65 male participants (26.2%) and 31 of the 53 female participants (58.5%) had been screened for STDs in the previous 12 months. Twenty of the male participants (30.8%) and 32 of the female participants (60.4%) had been screened for STDs in the previous 24 months. To control for the timing of first sexual intercourse, we examined the screening rates among male (n = 41) and female participants (n = 20) who had first engaged in sex 2 or more years before the interview and among male (n = 23) and female participants (n = 32) who had first engaged in sex less than 2 years before the interview. For male participants, there was no difference in the 2-year screening rate between those with less recent and those with more recent first sex (30.4% vs 31.7%; $P = 0.8$). For female participants, however, a difference was noted in the 2-year screening rate between those with less recent and those with more recent first sex (80.0% vs 50.0%; $P < 0.05$).

To answer the question of whether adolescents who are being seen for preventive primary care are also being screened for STDs, we focused on the 53 male participants and 40 female participants who had a preventive primary care visit after they first had sex. As a group, these adolescents reported receiving primary care at several different types of clinics, including both private and publicly funded sites. Among those adolescents who had had a primary preventive care visit, 14 of the male participants (26.4%) and 24 of the female participants (60.0%) had been screened for STDs at some time in the previous 24 months. Table 2 shows the percentage of participants screened according to selected STD risk factors. Eleven of the male participants (20.8%) and 16 of the female participants (40.0%) were screened for STDs during the pri-

Table 1 *Characteristics of sexually experienced male and female African American adolescent participants, San Francisco, 1997 (n = 118)*

Characteristics	Women (n = 53), No. (%)	Men* (n = 65), No. (%)
Age, yr		
12-14	12 (22.6)	7 (17.5)
15	9 (17.0)	5 (12.5)
16	11 (20.8)	14 (35.0)
17	21 (39.6)	14 (35.0)
Maternal education†		
Less than high school	8 (15.1)	6 (15.0)
High school	17 (32.1)	20 (50.0)
More than high school	28 (52.8)	14 (35.5)
History of at least 1 STD‡		
Yes	6 (11.3)	7 (17.5)
No	47 (88.7)	33 (82.5)
Lifetime number of sex partners		
1	12 (23.1)	24 (60.0)
2	8 (15.4)	4 (10.0)
3	11 (21.2)	3 (7.5)
≥4	21 (40.4)	9 (22.5)

STD = sexually transmitted disease
*25 male adolescents did not answer all questions, so the denominator is 40.
†Paternal education was substituted for maternal education for participants who did not live with their mother or a female guardian.
‡Ever diagnosed with or treated for chlamydia, gonorrhea, syphilis, pelvic inflammatory disease, or genital herpes.

Table 2 *African American adolescents who had a primary preventive health visit in past 2 years and were screened for a sexually transmitted disease (STD) according to selected STD risk factors, San Francisco, 1997*

Characteristics	Screened, No. (%) Men (n = 53)	Women (n = 40)
Age, yr		
12-14	12 (16.7)	7 (28.6)
15	9 (44.4)	5 (80.0)
16	11 (27.3)	14 (50.0)
17	21 (23.8)	14 (78.6)
History of at least 1 STD*		
Yes	6 (33.3)	7 (71.4)
No	47 (25.5)	33 (57.6)
Lifetime number of sex partners		
1	12 (41.7)	24 (54.2)
2	8 (12.5)	4 (75.0)
3	11 (36.4)	3 (33.3)
≥4	21 (19.1)	9 (77.8)

*Ever diagnosed with or treated for chlamydia, gonorrhea, syphillis, pelvic inflammatory disease, or genital herpes.

mary preventive care visit. The small number of sexually experienced adolescents who had received a preventive primary care visit precluded us from using inferential statistics to test for differences in screening rates according to STD risk factors.

DISCUSSION

The results of our study indicate that sexually experienced African American adolescents living in a low-income area of San Francisco are being screened for STDs at rates below those recommended by current practice guidelines. Even adolescents who receive primary health care are not being screened at the recommended level. These findings are of particular concern because the adolescents in our study are among the highest risk group for STDs in the United States. They are low-income African American adolescents who live in a neighborhood with a high prevalence of STDs.

The low rates of screening for STDs may be related to any of the potential hurdles that need to be crossed before an STD screen occurs. First, clinicians need to take a sexual history. One study found that about 75% of California physicians report that they routinely take a basic sexual history from adolescents,[9] whereas another found that only 40% report doing so.[10] In some cases, adolescents may be unwilling to disclose the truth, particularly if the physician does not make assurances about protecting confidentiality.[11] Also, even if a physician determines that an adolescent is sexually experienced, the physician may still not do an STD screening examination owing to a lack of awareness of current screening guidelines[12] or to feeling incompetent to perform an STD screen.[13] In some cases, adolescents may refuse to be screened for STDs.

The method of our study has limitations. Adolescents may not have been honest in their responses about their sexual behavior and their STD history because of the sensitivity of the data.[14,15] Because of this concern, our interviewers were careful to reassure adolescents that all responses were confidential. Also, all questions were pilot tested and were worded such that they could be answered with only a "yes" or "no" or with a number to prevent a household member from understanding an adolescent's responses. Despite these efforts, adolescents may have overreported or underreported their sexual behavior and STD history.[14,15]

Also, some male adolescents may have been screened for an STD by leukocyte esterase testing of a urine specimen without being aware of it, thus falsely lowering self-reported rates of STD screening.[16] This scenario is not likely to be true for female adolescents. Because urine-specimen–based screening of women was not routinely available at the time of the survey, an adolescent girl would likely have realized that she had an STD screening test because it required a pelvic examination. But an adolescent girl may have thought she had been tested for STDs when she had not. For example, the clinician may have only collected a cervical smear for a Papanicolaou test, but the adolescent thought that she had had an STD screening test. Thus, female adolescents may have overreported being screened for STDs.

A further limitation of our study is that we surveyed only African American adolescents who live in a small geographic area. Certainly, knowing the proportion of all American adolescents that is being screened for STDs would be ideal. In the absence of data from a nationally representative sample, however, we believe it is informative to collect data from smaller populations of adolescents and, in particular, those who are at highest risk for acquiring an STD.

In summary, African American adolescents are being screened for STDs at a rate below that recommended by current practice guidelines. The preventive primary care visit is not being used to its full potential as a valuable opportunity to screen adolescents for STDs. Capitalizing on this opportunity may increase rates of STD screening and, thus, decrease rates of STDs in adolescents. One hope is that recent technologic advances in the diagnosis of STDs—that is, urine-specimen–based STD testing—may increase both clinicians' willingness to screen and adolescents' willingness to be screened for STDs and, thereby, increase the number of adolescents screened for STDs.

We would like to dedicate this manuscript to the memory of Karen Garrett, whose commitment to the implementation of the project ensured its success.

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COMMENTARY

The race of patients and physicians can affect the quality of health care provision

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Ellen and colleagues' study indicates a low screening rate for a high-risk population. These findings are alarming because the need for consistent screening of adolescents has been repeatedly established.

One study of inner-city adolescent females concluded that they should be screened for chlamydia every 6 months, based on the incidence of this infection in the study population.[1] Another study also suggests an optimal screening interval of 6 months, based on high STD prevalence and incidence despite moderate risk behavior, such as only 1 lifetime sexual partner.[2]

Ellen and associates found a low rate of STD screening even among adolescents attending for primary care visits. This is consistent with other reports of poor rates of screening and delivery of preventive services to adolescents in a variety of clinical settings, including primary care visits.[3,4]

As health care physicians for a substantial African American population in the Adolescent Medicine clinic of Children's Hospital, Oakland, California, we believe that a major barrier to adequate STD education and screening in adolescents is physicians' failure to discuss sexuality. This failure occurs despite well-documented guidelines, such as the American Medical Association's Guidelines for Adolescent Preventive Services (GAPS), and screening and assessment tools, such as the "HEADS" psychosocial assessment—home environment, education, activities and employment, peer activities, drugs, sexuality, and suicide.[5] A recent study of California primary care providers showed that less than 40% of physicians asked all of their adolescent patients about sexual activity.[3] Appropriate STD screening cannot be performed without taking an adequate sexual history. The preventive primary care visit is just 1 of many opportunities to obtain sexual histories and perform appropriate screening. The philosophy at our clinic is to use every visit as an opportunity to discuss issues related to sexuality and to screen for STDs, if indicated. This requires flexibility in the physician's schedule because a visit for a minor respiratory tract infection might turn into a lengthier STD screening.

In the African American population studied by Ellen and colleagues, there may have been inherent barriers to the delivery of primary health care services. As a group composed primarily of African American health care providers, we find it interesting that the authors did not comment on the role that race itself may have had in determining health care access and delivery, despite the fact that the study focused exclusively on African American adolescents. Race may have been a major barrier to the delivery of primary care services to the study population. The race of patients and providers affects quality of care, access to care, health care service provision, and screening.[6-8] Provider attributes, including race, can undoubtedly influence patients' use of health care. Black patients are more likely to report having received preventive and other medical care, and to rate their physician as excellent, if their physician is also black.[8] There is increasing evidence of the importance of such racial concordance in ensuring access to and continuation of health care.[9] It is reasonable to assume that screening rates for African American adolescents might have been higher if they had been given access to African American providers. At the very least, the issue of racial concordance and discordance should have been explored and discussed.

In another article in the same study population, it was reported that African American teens placed the greatest importance on provider attributes when deciding to seek STD care. Provider attributes did not include race but

focused on those characterized primarily as behavior.[10,11] It is critical to explore the effect of provider race as one of the provider attributes. We encourage health care professionals to consider these issues when caring for adolescent patients.

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A Book That Changed Me

Understanding today's Joads: revisiting *The Grapes of Wrath* by John Steinbeck

Like all great books, Steinbeck's *The Grapes of Wrath* absorbs and entertains but also alters our perspective on life. Its principal theme is intolerance, its uncomfortable lesson is that prejudice lies beneath the surface of us all, but its optimistic conclusion is the courage of the human spirit and the kernel of good that remains when all else is stripped away. The poetic style and vernacular dialogue take time at first, but once it hooks the reader, it won't let go.

It is the story of the Joad family—Oklahoma farmers whose lives are ruined by the Dust Bowl of the 1930s. Forced from their land and fueled by their belief in the "American dream" of opportunity, they travel west to California. They endure dreadful hardship on the way, and when they arrive, their optimistic hopes and dreams are shattered by the hostility they encounter.

Steinbeck's greatest skill is showing how the Joads engender this hostility, prickling our own innate prejudices. They are crude, crassly naive, violent, and hypocritical. They seem unable to make the link that they are being driven from the land as their forefathers drove the native Indians from it. Yet, once the reader gets to know them, feel the pathos of their humanity, and share their experience, it is impossible not to become deeply attached and then appalled not only at the treatment they receive but also at our own initial prejudicial reaction.

I have just reread the book after 20 years, and its relevance persists. The homeless, travelers in their caravans, asylum seekers, and refugees are all today's Joads.

Throughout the novel, Steinbeck parodies faith that has no moral depth. He uses many biblical themes and images, and some passages of the book are written in a quasi-scriptural tone. The Bible developed out of a collective human need to give life context, meaning, and a moral structure, but Steinbeck suggests that this message, along with its contemporary relevance, has been lost. In a secular, multicultural age, *The Grapes of Wrath* shows that storytelling remains (next to life itself) the preeminent form to teach us about ourselves and our world. It is a book that teaches empathy, compassion, and tolerance. But perhaps its greatest lesson is that these things need to be taught, and constantly retaught, to us all.

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Journal Digest

In patients with acute bronchitis, do antibiotics reduce sputum production, cough, or number of days off work?

Bent S, Saint S, Vittinghoff E, Grady D. Antibiotics in acute bronchitis: a meta-analysis. *Am J Med* 1999;107:62-67.

DATA SOURCES

English-language studies were identified in MEDLINE (1966-April 1998) by using the terms drug therapy, bronchitis, and acute disease; the reference lists of relevant articles were reviewed, and experts in the field were contacted.

STUDY SELECTION

Studies were selected if they were randomized controlled trials that compared the use of antibiotics with that of placebo in patients who had acute bronchitis but no history of chronic lung disease or pneumonia, therapy was given for 5 days or longer, and effect sizes could be calculated from the data presented.

DATA EXTRACTION

Data were extracted on sample size, patient age, study inclusion and exclusion criteria, antibiotic regimen, and outcome measures. The main outcome measure was days of sputum production, which was transformed into SD units for each study.

MAIN RESULTS

Eight studies (660 patients) were included and used erythromycin, doxycycline, or the combination of trimethoprim and sulfamethoxazole. The overall summary effect size of antibiotic therapy was 0.21 SD units (95% confidence interval, 0.05-0.36), equivalent to about a half-day less of cough and sputum production than with placebo. Days of purulent sputum, days of cough, and days lost from work were measured in 4 or more trials; the results for antibiotic use and placebo did not differ (table).

Antibiotics vs placebo for outcomes of acute bronchitis measured by 4 or more trials

Outcomes	No. of trials	Weighted mean decrease (95% CI), d
Day of purulent sputum, No.	6	0.4 (−0.1–0.8)*
Days of cough, No.	4	0.5 (−0.1–1.1)†
Days off work, No.	6	0.3 (−0.6–1.1)†

CI = confidence interval.
*Significant when pooled in SD units, but not significant in units of days.
†Heterogeneity existed among these studies. Results were not significant.

CONCLUSION

In patients with acute bronchitis, the use of antibiotics reduces cough and sputum production by about half a day.

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Commentary

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The systematic review by Bent and colleagues shows that antibiotics have marginal benefit in the treatment of adults with acute bronchitis. The results are consistent with those of 2 previous systematic reviews.[1,2] Acute bronchitis is not a trivial illness; for most adults, it lasts ≥3 weeks and has a major effect on patients' well-being and daily activities.[3] This review suggests that antibiotics may shorten the duration of illness by half a day; but when side effects, costs of treatment, and the "medicalizing" effects of antibiotics are considered, the risks associated with treatment seem to outweigh the benefits.

No symptoms or signs definitely rule in a bacterial diagnosis. It appears that patients' expectations substantially affect the prescribing of antibiotics by family physicians.[4]

In addition to evidence about the effectiveness of antibiotics, management strategies used to reduce prescribing and to meet patients' expectations are needed. A United Kingdom randomized trial is currently evaluating the effectiveness of offering each patient a delayed antibiotic prescription. Furthermore, a patient information leaflet has been shown to be effective for reducing repeated consultations and providing patients with information about the likely course of their illness.[5]

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Does attendance at a general practice asthma clinic reduce asthma morbidity more than does standard medical treatment?

Heard AR, Richards IJ, Alpers JH, et al. Randomized controlled trial of general practice based asthma clinics. *Med J Aust* 1999;171:68-71.

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DESIGN

6-month, randomized, unblinded,* controlled trial.

SETTING

8 general practices in South Australia.

PATIENTS

195 patients aged 5 to 64 years (mean age, 26 years; 55% women) who had asthma. Follow-up was 98%.

INTERVENTION

Patients were allocated to a group attending an asthma clinic (n = 98) or to a standard treatment group (n = 97). Asthma clinics operated once per week for a 3-hour session. Registered nurses with extensive respiratory care experience educated patients in asthma management strategies, including a written asthma management plan; spirometry; and use of peak flow meters, inhalers, and asthma diary cards. Patients in the asthma clinic group were asked to attend 3 sessions.

MAIN OUTCOME MEASURES

Days missed from work or school; use of an action plan; medication use; current smoking; level of morning or nocturnal asthma symptoms; and number of hospitalizations, emergency department visits, and home visits by general practitioners.

MAIN RESULTS

Of the 98 patients allocated to the asthma clinic group, 67 attended 3 sessions, 17 attended 1 or 2 sessions, 13 attended no sessions, and 1 patient withdrew. Analysis was by intention to treat. The study had 80% power to detect a 50% reduction in the proportion of patients reporting 1 day or more lost from work. At 6 months, patients in the asthma clinic group were more likely than patients in the standard treatment group to own a peak flow meter and less likely to be awakened at night because of asthma (table). A trend existed for more patients in the asthma clinic group to begin or recommence smoking (table). The groups did not differ for any other outcomes.

*Information provided by author.

Asthma clinic vs standard medical treatment for asthma morbidity at 6 months

Outcomes	Asthma clinic	Standard care	RBI (95% CI)	NNT (CI)
Owning a peak flow meter	73%	56%	30% (5%-62%)	6 (3-31)
			RRR (CI)	
Waking at night because of asthma	7%	20%	64% (21%-84%)	8 (4-29)
			RRI (CI)	**NNH (CI)**
Currently smoking	15%	7%	108% (−8.5%-378%)	Not significant

RBI = relative benefit increase; RRR = relative risk reduction; RRI = relative risk increase; NNT = number needed to treat; NNH = number needed to harm; CI = confidence interval.

CONCLUSIONS

Patients with asthma who attended a general practice asthma clinic were more likely to own a peak flow meter and less likely to wake at night because of asthma than those receiving standard medical treatment, but they did not differ for any other measures of asthma morbidity.

Commentary

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Advances in medicine have led to improved outcomes for many diseases, but the burden of suffering from asthma is increasing. Current efforts to reduce the morbidity from asthma focus on better delivery of care and patient education. Such interventions as asthma clinics and home visits are now common.

Heard and colleagues have shown that an asthma clinic in addition to routine physician care has little effect. They point out, however, the limitations of the study. First, control and intervention-group patients were often seen by the same physician who, aware that his or her practice behavior was under scrutiny, may have provided more conscientious care than usual. Second, Heard and colleagues studied mostly patients with less severe asthma, as reflected by the low hospitalization rate in both groups. Third, the study was small, and many patients did not complete the asthma clinic intervention. Given these shortcomings, it is impossible to conclude that asthma clinics in general are not useful. Other interventions, including home visits and community outreach programs, have substantially improved patient education and such cost-sensitive outcomes as emergency department visits.[1,2] Heard and colleagues show that general practitioners, under the right circumstances and with some incentive, are able to provide quality asthma care and education. The best targets for new asthma programs are perhaps the physicians themselves.

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Best Practice

TOPICS IN REVIEW

Hope in the terminally ill

Hope is the wings upon which the future soars.

ANONYMOUS

INTRODUCTION

The diagnosis of a terminal illness initially precipitates a vulnerability and isolation that belie description as contemplation of one's impending death transcends the mundane activities of daily living. Mortality is suddenly confronted, and the concept of hope wanes as the unattainable goal of extended life vanishes. And while denial may temporarily intervene and preclude reality, the fact that life is ending becomes hard to deny as the disease advances. But a seemingly paradoxic question arises: because hope is frequently defined as the expectancy of good in the future, how can a future defined in hours, days, weeks, and months provide hope?[1] To understand the answer to this contradictory question, physicians must acknowledge the dynamic and complex nature of hope and how it changes during the dying process.

REPORT OF A CASE

Mrs Brown was a 69-year-old widow with metastatic breast cancer and with no known family. Although she had undergone chemotherapy and radiotherapy, the disease progressed relentlessly. Her oncologist proposed another chemotherapy regimen using a new agent with substantial adverse effects. After 3 episodes of the new chemotherapy, Mrs Brown was debilitated, emaciated, depressed, and hopeless. The oncologist suggested a break from treatment for 3 to 4 weeks to allow her nutritional and functional status to improve, after which chemotherapy could be reinstituted.

In the interim, the patient was enrolled in a hospice progtam. The hospice staff developed rapport with her, assisted her with a life teview, discussed the terminal nature of her disease, and discovered that she was estranged from a daughter she had not seen in 30 years. After diligent labor, the hospice social worket located the daughter and arranged for a meeting at the patient's home. Mrs Brown's spirit improved; she was excited about the impending visit with her daughtet and elected not to proceed with chemotherapy, considering the extent of her disease and the adverse effects of the treatment. The false hope of a relatively futile medical intervention (chemotherapy) was replaced with an appropriate and humane hope of reconciling with a long-lost daughtet, resolving familial discord, and experiencing an improved quality of life.

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Sam Tanner/Photofusion

Encouraging lightheartedness and humor, when appropriate, can engender hope in terminally ill patients

Interventions that engender hope[1,8]

- Adequate control of symptoms
- Fostering and developing interpersonal connectedness and relationships
- Assistance in attaining practical goals
- Exploring spiritual beliefs
- Supporting and identifying personal attributes, such as determination, courage, and serenity
- Encouraging lightheartedness when appropriate
- Affirming worth by treating the patient as a valued individual
- Recalling uplifting memories with life review

THE MEANING OF HOPE

Unfortunately, physicians often consider hope and terminal illness mutually exclusive. Many equate hope with cure in the archetypal disease-illness paradigm and may express this notion to patients.[2-4] As Nekolaichuk and Bruera note, people who are terminally ill often become marginalized from mainstream society.[2] This marginalization is associated with existential distress, social isolation, and loss of familial and occupational roles, which can further dissipate hope.

When first confronted with a terminal illness, most patients typically relate hope to a tangible treatment or cure that can prolong existence despite overwhelming information to the contrary. Part of this illogical hope may derive from inappropriate information given by physicians to patients when delivering bad news. Physicians are characteristically hesitant to deliver devastating news and may abstain from truth telling in an effort to sustain and bolster hope. They frequently temper the diagnosis of a terminal illness with unrealistic and unintentional "therapeutic" hope. Such misguided hope may involve telling patients about futile treatments such as chemotherapy, radiotherapy, and surgery, which can create false expectations. It may also help physicians to deal with their feelings of impotency in the face of a relentless disease and certain death.[3] As Brody noted, however, an accurate disclosure of the truth can almost always be coupled with an element of hope.[5] Physicians are persuasive modulators of patients' hope.[6] Practitioners who care for patients with terminal and life-threatening disease face the challenge of balancing honest communication with maintaining hope.[7]

After patients' initial anguish at the news of their terminal illness, the future often becomes defined by family, close friends, and the meaning attached to life, rather than to the length of time remaining. Patients' thoughts and concerns become more global as they envisage, and hope for, a positive outcome for their family and friends. Then, as death approaches, patients often focus on themselves, expressing a desire for serenity, inner peace, and eternal rest.[1]

DETERRENTS TO HOPE

Unfortunately, deterrents to hope may exacerbate the fear and trepidation surrounding dying and preclude a peaceful and tranquil death. In a study by Herth, 3 obstacles hindered hope: abandonment and isolation, uncontrolled pain, and devaluation of personhood.[1] Herth identified 4 sources of hope, including family, friends, health care professionals, and God or a higher spiritual being. Because health care professionals are a source of hope, they must remember that specific strategies foster and maintain hope in their patients. Aside from compassionate disclosure of the diagnosis of a terminal illness, physicians can engender hope through various mechanisms (see box). Life review, in which patients recount their lives, jobs, travels, and experiences, is a simple and important intervention to help patients achieve purpose and meaning at the end of life. Nuland proposes that hope resides in the meaning of what our lives have been.[3]

CONCLUSION

Hope is the expectancy of good in the future. It plays a role in the successful coping with illness and in improving the quality of a person's life. In the context of a terminal illness, hope can exist even when time is limited. Such hope is bolstered by appreciating our patients' value, strengthening and reconciling their relationships with family and friends, helping them to explore spiritual matters, and controlling their symptoms. Although physicians may find it hard to comprehend, when everything seems to be lost, that hope may actually be stronger than ever before.

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From the cell to the community: AIDS research in California

The University of California Universitywide AIDS Research Program annual meeting, February 2000

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INTRODUCTION

Between 1981 and 1999, more than 110,00 cases of the acquired immunodeficiency syndrome (AIDS) have been reported in California, of whom nearly 70,000 patients have died. Since 1983, the University of California has funded basic, clinical, social, and behavioral research on the human immunodeficiency virus (HIV)/AIDS through the Universitywide AIDS Research Program (UARP). Major accomplishments of UARP-supported research include the isolation and characterization of HIV, the detection and elimination of HIV in blood clotting factor VIII, and in early studies, the demonstration of the rapid production and turnover of HIV in the blood of infected persons.

Together with its advisory group, the Universitywide Task Force on AIDS, UARP convenes an annual meeting that provides an opportunity for the exchange of new information on HIV/AIDS in California. Participants include bench scientists, clinicians, policymakers, outreach workers, community-based organizations, and members of affected communities. Most of the studies presented at the UARP conference are in their early stages and modestly funded. While some go on to receive larger federal grants, others are quickly integrated into new interventions or investigations.

In this issue of *wjm,* we share highlights of the 3rd Annual Conference on AIDS Research in California.† The plenary theme for the year 2000 was "Early Events and Intervention in HIV Infection." Although the recent and ongoing advances in highly active antiretroviral therapy are well known, the meeting provided a fertile venue for presenting other innovative areas for treatment and prevention.

FEATURED SPEAKER HIGHLIGHTS

Primary HIV infection in high-risk populations: the options project

Presenter: James O Kahn

Primary HIV infection refers to the clinical events that occur within 12 months of becoming infected. Clinicians should think of primary HIV infection as a diagnosis in patients who may have been exposed to the virus and who present with rash, fever, myalgia, pharyngitis, or other features of a viral illness. Such patients should be screened for HIV-1 RNA and antibody using the enzyme-linked immunosorbent assay (EIA). Early therapy with protease inhibitors used in combination with other antiretroviral agents can control HIV during the earliest, acute phase of infection. However, identifying individuals in the community who have recently become infected is very difficult.

Patients with primary HIV infection are at high risk of transmitting HIV infection to others. In the absence of antiretroviral therapy, levels of HIV RNA are often very high during acute HIV infection and can reach above 10^6 copies per milliliter. Previous studies suggest that the level of HIV RNA is important in transmission.

The Options Project, a collaboration of University of California scientists, exemplifies UARP's approach of targeting research "from the cell to the community." This research brings together basic, clinical, and behavioral scientists who are interested in primary HIV infection. The collaboration addresses a number of key questions (see box).

In the Options Project cohort study, patients with signs or symptoms of primary HIV infection are screened to assess their HIV antibody and viral RNA status. Patients either refer themselves, or they are referred by clinicians, community-based organizations, emergency departments, or HIV test centers. Enrollment into the study is

Summary points

- Antiretroviral therapy should be maintained, even in the face of drug resistance and a detectable HIV viral load
- Postexposure prophylaxis with antiretroviral therapy may reduce the likelihood of HIV infection within 72 hours of a high-risk encounter and is not likely to encourage subsequent risky behavior
- Any suspected primary HIV infection requires laboratory screening; the HIV RNA assay is more sensitive, but the p24 antigen assay offers fewer false-positives
- Socially disadvantaged African American youth and men continue to be at especially high risk for sexually transmitted diseases and HIV and can benefit from counseling and screening
- Injection drug users (IDUs), especially those participating in syringe exchange programs, are often motivated by friendship and altruism to exchange needles for other IDUs; these qualities may make them good candidates for communicating HIV prevention messages among their networks

*Affiliations are listed on p 124

†More detailed descriptions of each conference project, including quantitative data, are contained in the Compendium of Abstracts (available at www.ucop.edu/srphome/uarp) or on request to Universitywide AIDS Research Program, 300 Lakeside Dr, 6th floor, Oakland, CA 94612-3550, attn: Denise Elkins.

The Options Project: key research questions

- What are the key ways that people present with HIV?
- In what ways are infected people different from the uninfected?
- How can we prevent HIV infection?
- Among newly infected persons, what are the recent virologic events and can they predict later events?
- What are the immune responses during infection?
- How can we intervene toward better outcomes?

ongoing. The project at the San Francisco General Hospital identifies newly infected patients and brings them into primary care while also observing patients who erroneously believe that they are infected. Most participants are men who have sex with men, and more than half have a history of substantial alcohol and drug use.

Of 310 patients screened to date, 122 with primary HIV infection have been identified. Infected participants were more likely to have had high-risk sexual behaviors than those who were uninfected. They were also more likely to have had depression and to have had a history of sexually transmitted diseases (STDs). One third of patients with primary HIV infection believed that combination therapy for HIV would prevent transmission to an uninfected person.

The Options Project has also monitored whether the viral strains in primary HIV infection are remaining susceptible to antiretroviral therapy. Although the number of isolates was relatively small, the proportion of patients whose HIV strain was resistant to zidovudine fell from 16% in 1996 to 3% in 1999, whereas the proportion resistant to protease inhibitors increased from 0% to 7.7% during the same period. Monitoring those with acute HIV infection remains an optimal method of assessing trends in the transmission of resistant virus.

The project team has evaluated patients with primary HIV infection or high-risk sexual behaviors during the course of their acute infection. With the benefit of counseling interventions in this cohort study, the practice of insertive anal intercourse with or without a condom decreased, but 50% of respondents continued to report high-risk activities. Providing early antiretroviral therapy to prevent immune destruction in patients identified with primary HIV infection is necessary but not sufficient to eliminate the virus. Behavioral modification strategies must also be included to reduce the risk of HIV transmission.

Further reading

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Treating high-risk populations with postexposure prophylaxis

Presenter: Mitchell H Katz

Postexposure prophylaxis may be one way of reducing new infections among persons who have engaged in a risk behavior with someone known to be or suspected of being infected with HIV. Postexposure prophylaxis involves providing combination antiretroviral therapy (Combivir [zidovudine, 300 mg, and lamivudine, 150 mg]) to exposed persons within 72 hours of the initial exposure for a 28-day course.

A recently completed project in San Francisco is addressing the feasibility of postexposure prophylaxis. This nonrandomized observational study enrolled 401 persons who sought postexposure prophylaxis, more than 90% of them for a sex-related exposure. Most participants were aged 31 to 50 years, 90% were men, and 69% were white. The cohort was observed and assessed at 1, 2, 4, and 26 weeks after intake. Risk reduction and medication adherence counseling was provided at several sessions, and patients were encouraged to bring in source partners for assessment.

Postexposure prophylaxis is useful only if the source partner is HIV-positive, but the partner's serostatus was unknown to 57% of participants. Clinicians should use community levels of HIV prevalence in deciding whether postexposure prophylaxis is appropriate for patients. The most important issue in this decision is the likely risk factors of the source partner, if known.* In areas such as San Francisco and Los Angeles, postexposure prophylaxis is advisable if the source is an IDU or a man who has sex with men because the prevalence of HIV in these cities is 5% to 10% in IDUs and 20% to 30% in men who have sex with men.

Patients using postexposure prophylaxis experience considerable subjective toxic reactions—nausea, anorexia, headache, fatigue—but virtually no safety issues, as demonstrated by laboratory values. From a public health perspective, postexposure prophylaxis is less cost-effective than behavioral counseling or condom distribution, but from a clinical perspective, it makes sense and it does not appear to enhance behavioral risk. Postexposure prophylaxis provides an opportunity to work with patients on current and future risk status, to evaluate for other STDs,

*The absolute prevalence level at which postexposure prophylaxis should be prescribed is unclear, although many physicians suggest between 1% and 5%.

and to immunize for hepatitis B. These patients do not want to be infected and are highly motivated to examine their behavior.

Serious questions still facing the project team include: how can clinicians encourage use of postexposure prophylaxis among racial and ethnic minorities (only 18% of patients seeking postexposure prophylaxis have been either Latino or African American) or among IDUs? Is it efficacious at preventing HIV infection? How can we prove it? Such challenges are to be expected of any HIV prevention strategy.

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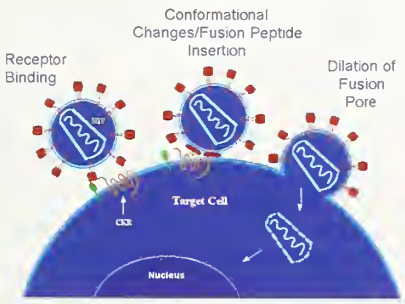
Viral fusion: the scientific underpinnings of early HIV infection

Presenter: Eric Hunter

Although several kinds of antiretroviral therapies are currently available, cellular entry by HIV is a compelling target for a new class of antiretroviral agents.

Three possible targeting strategies may lead to new therapeutics directed against viral entry into the cell:

- Disrupting binding of CD4 (a molecule on the helper T-cell surface) to gp120 (the membrane protein of HIV) through direct antagonism at the interface because the CD4 protein serves as a gatekeeper to viral entry into the cell.
- Preventing engagement of a cellular chemokine receptor or "coreceptor" through agents that bind to key sites on the coreceptor, the primary cellular cofactor for HIV entry.
- Interfering with fusion by using peptides or small molecules to disrupt the structure or dynamics of gp41 (the exterior or envelope protein of the virus that facilitates fusion with the cell).



Conformational changes in envelope allow cellular entry by HIV

The third strategy may be the most promising for blocking viral entry into the cell and is now being tested in clinical studies.

In a Phase I/IIB clinical trial, researchers at the outpatient clinic of the University of Alabama, Birmingham, Medical Center gave a prototypical peptide antagonist of HIV entry intravenously twice a day in the clinic to 16 HIV-infected patients in 4 dose groups (3, 10, 30, and 100 mg twice a day) for 14 days. Patients had a dose-dependent reduction in viral load, achieving as high as a 2-log effect, suggesting that HIV could be reduced to preclinical levels. Frequent intravenous administration may not be necessary; intermittent subcutaneous infusions may effectively reduce viral load. These studies suggest that viral fusion is a viable target for the design and development of new treatment strategies. They also illustrate the way in which basic research may have immediate clinical implications.

Second-generation peptides with improved pharmacologic properties are also undergoing clinical trials. Meanwhile, a major goal is the development of small-molecule antagonists that will similarly disrupt the viral fusion process. Initial clinical tests of fusion inhibitors suggest that disrupting the binding process will be clinically useful.

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CURRENT QUESTIONS IN HIV/AIDS RESEARCH IN CALIFORNIA

Clinical sciences

Progress in clinical research has resulted in an increase in survival and quality of life for people with HIV/AIDS. A current priority is to unite the growing understanding of the molecular underpinnings of the virus and the increased use of antiretroviral drugs with progress in diagnosis and treatment. Changes in treatment have led to 5 important clinical questions.

1. Which laboratory tests and symptoms are most predictive of primary HIV infection?

Symptomatic (n = 436) and asymptomatic (n = 69) subjects with recent exposure to possibly HIV-infected persons were screened for primary HIV infection, and their symptoms were recorded. Researchers compared 2 different methods of detecting recent HIV seroconversion. Plasma HIV RNA testing was compared with p24 antigen (p24 is a structural protein of HIV) in differentiating primary HIV infection in those whose

ELISA screens were negative or whose Western blot screens were indeterminate (these 2 are standard HIV screens). The p24 antigen was almost as sensitive as the HIV RNA test and had the extra advantage of fewer false-positives in patients ultimately found to be negative for HIV.

The following symptoms occur more commonly in patients with primary HIV infection than in those who are uninfected or chronically infected: fever, myalgia, arthralgia, rash, night sweats, and pharyngitis ($P < 0.05$). But no constellation of symptoms was sufficiently sensitive or specific to predict primary HIV infection without laboratory screening.

2. Why do a subset of patients with primary HIV infection have reduced antiviral drug susceptibility?

One theory is that these patients share a common source of infection, perhaps because they come from the same region. But preliminary results on 49 patients, for whom therapy with 1 class of antiretroviral agents failed, provide no evidence for this theory. Using molecular epidemiologic techniques, the authors found no evidence suggesting clustering of viral nucleotide sequences, and they concluded that the cases did not appear to be linked by person, place, or time.

3. What are the pros and cons of interrupting antiretroviral combination therapy?

Should antiretroviral therapy be continued even if there is evidence of viral failure? A randomized study of 18 patients showed that the continuation of antiretroviral therapy has clear benefit, even if it appears not to be working well, as evidenced by increased viral load. Patients who were continued on therapy were often found to maintain stable CD4 cell counts despite virologic failure. For those discontinuing antiretroviral therapy, CD4 counts fell substantially by 12 weeks, in addition to an increase in viral load. These results suggest that continuing protease inhibitor–based antiretroviral therapy, despite the apparent treatment failure indicated by a rebound in viral load, has a beneficial effect in many patients because the therapy selects for less virulent HIV strains. The investigators hypothesized that this is possibly due to a weakened virus; thus, when the virus mutates and becomes resistant to protease inhibitor–based therapy, it does so at the cost of reduced virulence.

4. Can a Web-based surveillance system be useful for ascertaining changes in response to treatment?

A team at San Francisco General Hospital is observing a prospective, observational cohort of patients receiving care from the Positive Health Program (PHP) using a database on the Web. The goal is to provide rapid, "real-world" evaluation of current treatment guidelines. The high-need PHP population is 17% women, 5% of the patients are unstably housed, and 65% receive Medi-Cal or Medicare. The patient group is 50% white, 30% black, 15% Latino, and 5% Asian. Between 1996 and 1998, the mean CD4 cell count increased. However, more than half of the patients had never achieved consecutive HIV RNA levels below the limits of detection. This could be an indication that for a large proportion of patients in clinical practice, current antiretroviral regimens may be failing and that the prevalence of HIV resistance to agents might be high.

5. How do characteristics of the HIV-1 envelope gene affect perinatal transmission?

A better understanding of how HIV-1 is transmitted to infants will guide the development of preventive therapy. A preliminary study suggests that there are differences in the level or degree of diversity of the HIV-1 envelope gene between infected mothers who do (n = 23) and those who do not (n = 36) transmit HIV to their infants in utero versus intrapartum. Researchers measured HIV-1 envelope gene diversity in women during gestation and at delivery and, in infants, at the first time testing positive and at age 12 weeks. They were able to sequence the gene and group its variants by frequency, showing that gene diversity differs for in utero and intrapartum transmission, and pointing the way to different strategies for interrupting viral transmission. They found that women transmitting HIV to their infants had significantly lower HIV strain diversity at delivery than nontransmitting women.

Social/behavioral and public health sciences

A growing diversity of subpopulations has been affected by HIV, as shown by the increasing proportion of AIDS cases in California among African Americans, Latinos, women, and persons who inject drugs. Developing strategies for changing highly personal and often stigmatized behaviors across a growing number of subgroups pose a challenge for public health researchers. Participants in the annual meeting were given a number of insights into the nature of this challenge.

1. Can HIV risk be modified in socioeconomically disadvantaged populations?

Sharing of drugs and injection equipment is an important survival tactic among homeless IDUs observed in a participant-observation field study in San Francisco. IDUs who share drugs and injection equipment can expect to receive assistance in the future from those they assist, leading them to share resources with other injectors to protect against possible future isolation when they are confronted with an emergency shortfall of heroin. As a result, generosity and social group solidarity lead directly to health risk. The implications of such behaviors from a public health point of view are dire, although such acts are entirely rational to the IDUs in averting heroin withdrawal specifically and further impoverishment in general.

Low-income, disenfranchised African American men who have sex with men in the Tenderloin neighborhood

Jeff Schonberg

Sharing drugs and injection equipment is socially important to homeless drug misusers, despite its high risk. (Courtesy of Philippe Bourgois)

of San Francisco are engaging in high rates of unprotected anal intercourse, often without knowledge of their partner's serostatus. A convenience sample of these men (n = 246) was recruited through flyers. At least a third of the men reported recent unprotected sex, and half reported some significant deficiency in knowledge of how HIV is sexually transmitted.

Social disadvantage is associated with STDs and HIV infection. In another low-income neighborhood in San Francisco, African American youth have disproportionately high rates of STDs. A community-based peer-led prevention program has just begun enrollment with the goal of increasing screening and treatment among this high-risk population.

Street youth are at high risk for hepatitis B and hepatitis C, as well as HIV. A San Francisco project used street-based sampling to recruit 310 IDUs younger than 30 years. Data were collected through interviews and serologic assays. Young female IDUs, despite shorter injection histories than men, were just as likely to be infected with HIV and viral hepatitis as male IDUs, suggesting that they are a group at particularly high risk of viral infection.

Transgendered male-to-female sex workers are a population at very high risk for HIV infection. Of 244 male-to-female transgendered people referred for study by service agencies in Los Angeles, 58% were sex workers. The workers were much more likely to engage in insertive and receptive anal sex and to inject nonhormonal drugs. But in a multivariate analysis, Latino ethnicity, less than 12 years of education, and younger than 30 years were more predictive of HIV seropositivity than risk behaviors.

HIV risk remains high in economically disadvantaged groups. (Courtesy of Philippe Bourgois)

2. Which interventions engage HIV-affected communities?

Several investigators reported promising findings related to HIV prevention among socially disadvantaged populations, documenting important developments in risk reduction initiated by at-risk groups. A study of white and Latino gay male youth found that the prevalence of unprotected sex with partners not identified as the respondent' boyfriend was relatively low. In an analysis of recent sexual activity, less than 10% of a sample of 40 gay youth reported unsafe sex with a person not identified as their boyfriend. Rates of unprotected sex with boyfriends, however, continued to be high. A survey of 549 men who have sex with men recruited in parks, dance clubs, and bars found that although alcohol and drug use were widespread in the young men, substance use was not associated with HIV risk behaviors.

Three studies focusing on IDUs have shown that many of those, referred to as "secondary exchangers," who attend syringe exchange programs exchange needles for other IDUs who do not use such programs. This practice emerges naturally out of existing relationships and is typically done out of friendship and altruism. A pilot study of 369 IDUs in a community-based sample found that secondary exchangers are willing to and are effective at disseminating HIV prevention messages to their social contacts.

3. What are the challenges to developing effective interventions?

The RESPECT-2 study is a randomized controlled trial taking place in 3 urban publicly funded STD clinics among patients seeking STD examinations. It will test the efficacy of rapid HIV testing and counseling in preventing

the reoccurrence of STDs among clients of urban public health clinics. Although no outcome data are available to report, follow-up rates for 3- and 6-month interviews have been good: 87% and 79%, respectively. Determining the efficacy of innovative HIV testing and counseling procedures in public health clinics is of growing importance. Yet, replicating a proven community-level prevention intervention outside of a research environment poses a number of problems. A case study of barriers to implementation of an HIV prevention program for young gay men in a community setting showed problems such as developing user-friendly technical assistance, a high staff turnover in the community-based agency charged with implementing the intervention, and the need for ongoing intensive training of front-line staff.

One of the most successful interventions presented at the meeting was one initiated by the Forensic AIDS Project team. The team provides care to HIV-positive inmates in the San Francisco County Jail system. A convenience sample of 53 HIV-positive inmates was recruited during a 6-month period in 1999. Participants were primarily men, 59% were African American, and 30% were white. The study found that a higher percentage of HIV-positive inmates are receiving antiretroviral therapy in jail than similar populations receiving care in community clinics. The investigators also found that antiviral resistance is low in this population. These findings underscore the desire among disadvantaged groups to receive care. Ironically, as the authors point out, the only place where socially disadvantaged groups are guaranteed HIV treatment constitutionally is in jail.

CONCLUSION

An ongoing challenge for social and behavioral scientists and for society in general will be to develop strategies that reach the diverse populations at risk for HIV. The researchers at the 3rd Annual Conference on AIDS Research in California are aware of this challenge and are attempting to meet it in diverse and innovative ways.

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Babies and cream cheese

While on call one night, I was paged by a nurse about a neonate. The nurse asked if I could come and examine the baby, since the father was extremely worried. The reason? He had dropped cream cheese on the baby's head. Naturally, my first clinical question over the phone was, "Regular, soft, or whipped?" I made my way to the scene, where the anxious parent filled in the details. "I was trying to spread the cream cheese on a bagel," he said, "but it slipped from the knife." At this point, I had to use every ounce of energy to prevent from breaking out into uncontrollable laughter. I held myself back, however, and proceeded to assess the mechanism of injury. Fortunately, it was only soft cream cheese, and the baby survived the ordeal unscathed. I assured the father that the baby was fine, and that compared to the trauma of a normal spontaneous vaginal delivery, the baby's encounter with the fermented milk would not be a problem. I also told him that for this exact reason, as part of our normal anticipatory guidance to parents of newborns, we only recommend having *whipped* cream cheese in the house in order to prevent any serious injury to newborns.

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CLINICAL EVIDENCE

Infectious diseases: meningococcal disease

This article comes from *Clinical Evidence* (2000;3:350-357), a new resource for clinicians produced jointly by the BMJ Publishing Group and the American College of Physicians–American Society of Internal Medicine. *Clinical Evidence* is an extensively peer-reviewed publication that summarizes the best available evidence on the effects of common clinical interventions gleaned from thorough searches and appraisal of the world literature. It became available in the United States late last year. Please see advertisement for more information or, alternatively, visit the web site at www.evidence.org.

QUESTIONS: What are the effects of prophylactic antibiotics on risk of disease in people exposed to someone with meningococcal disease? What are the effects of antibiotics in people with throat carriage of meningococcal disease?

INTERVENTIONS

In descending order of effectiveness

Prophylactic antibiotics in contacts

Antibiotics for throat carriage (reduce carriage, but unknown effect on risk of disease)

Vaccines (monovalent/multivalent; polysaccharide alone, or conjugate)

Empiric treatment of suspected meningococcal disease

Treatment of meningococcal disease

DEFINITION

Meningococcal disease is any clinical condition caused by *Neisseria meningitidis* (the meningococcus) groups A, B, C, or other serogroups. These conditions include purulent conjunctivitis, septic arthritis, meningitis, and septicemia with or without meningitis.

INCIDENCE/PREVALENCE

Meningococcal disease is sporadic in temperate countries and is most commonly caused by group B or C meningococci. The incidence in the United Kingdom varies from 2 to 8 cases per 100,000 people per year[1] and in the United States from 0.6 to 1.5 per 100,000 population.[2] Occasional outbreaks occur among close family contacts, secondary school pupils, and students living in student housing. Sub-Saharan Africa has regular epidemics caused by serogroup A, particularly in countries lying between Gambia in the west and Ethiopia in the east (the "meningitis belt"), where the incidence during epidemics reaches 500 per 100,000.[3]

ETIOLOGY/RISK FACTORS

Meningococcus infects healthy people and is transmitted by close contact, probably by exchange of upper respiratory tract secretions (table 1).[4-12] Risk of transmission is greatest in the first week of contact.[7] Risk factors include crowding and exposure to cigarette smoke.[13] Children younger than 2 years have the highest incidence, with a second peak between ages 15 and 24 years. Currently an increased incidence of meningococcal disease is being seen among university students, especially among those in their first term and living in catered accommodations,[14] although we found no accurate numeric estimate of risk from close contact in, for example, halls of residence. Close contacts of an index case have a much higher risk of infection than people in the general population.[7,10,11] The risk of epidemic spread is higher with group A and C meningococci than with group B meningococci.[4,6,8] What makes a meningococcus virulent is not known, but certain clones tend to predominate at different times and in different groups. Carriage of meningococcus in the throat has been reported in 10% to 15% of people; recent acquisition of a virulent meningococcus is more likely to be associated with invasive disease.

PROGNOSIS

Mortality is highest in infants and adolescents and relates to disease presentation.[15-17] Case-fatality rates in septicemia range from 19% to 25%; in meningitis plus septicemia, from 10% to 12%; and in meningitis alone, less than 1%.[15-17]

AIMS

To prevent disease in contacts.

Summary points

- We found no randomized evidence about the effects of antibiotics on the incidence of meningococcal disease among contacts. Observational data suggest that antibiotics reduce the risk of disease. We found no good evidence to address the question of which contacts should be treated.
- Randomized controlled trials have found that antibiotics reduce throat carriage of the meningococcus. We found no evidence that eradicating throat carriage reduces the risk of meningococcal disease.

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Competing interests:
None declared.

Table 1 *Risk of infection among contacts*

Group of meningococcus	Setting	Relative risk (RR)
A	Household contacts in Milwaukee, WI[4]	AR 1,100/100,000; RR not possible to estimate
	General population in Santiago province, Chile, household contacts[5]	Attack rate in general population 23-261.6/100,000 (1941 and 1942) Attack rate in household contacts 250/100,000 (2.5%) over both years
	General population in Indianapolis, IN[6]	AR 4,500/100,000; RR not possible to estimate
B	Household contacts in Belgium[7]	RR 1245*
	Nursery schools[7]	RR 23*
	Day care centers[7]	RR 76*
C	Household contacts from 2 lower socioeconomic groups, Dade County, FL[8]	Attack rate in 2 communities, 13/100,000 population; attack rate in household contacts, 5/85 (582/100,000)
Unspecified	School-based clusters in US; predominant meningococcal types: 13 clusters of GpC, 7 of GpB, 1 of GpY, 1 of CpC/W135 (impossible to distinguish)[9]	RR 2.3*
	Household contacts from several states in US, meningococcus types B and C predominantly[10]	RR 500-800*
	Household contacts in Norway; meningococcus types A, B, and C predominantly[11]	RR up to 4,000*
	Schools; predominant meningococcus type C[12]	OR 14.1 (95% CI, 1.6-127)

AR = absolute risk; OR = odds ratio; CI = confidence interval.
*Compared with the risk in the general population.

OUTCOMES

Rates of infection, rates of eradication of throat carriage, and adverse effects of treatment.

METHODS

The author searched by MEDLINE and BIDS in December 1998 and drew from a collection of references from the pre-electronic data era. All studies were considered for inclusion. *Clinical Evidence* search and appraisal November 1999.

QUESTION: What are the effects of prophylactic antibiotics on the risk of disease in people exposed to someone with meningococcal disease?

We found no randomized evidence of the effects of antibiotics on the incidence of meningococcal disease among contacts. Observational data suggest that taking antibiotics reduces the risk of disease. We found no good evidence to address the question of which contacts should be treated.

Benefits

We found no systematic review and of randomized controlled trials (RCTs) examining the effect of prophylactic antibiotic use in people who have been in contact with someone with meningococcal disease. **Rifampin [Rifampicin]:** We found only anecdotal data. **Penicillin:** We found 1 retrospective study whose results cannot be generalized beyond the sample tested.[18] **Sulfadiazine:** One observational cohort study of soldiers in temporary troop camps in the 1940s compared the incidence of meningococcal disease in camps where sulfadiazine was given to everyone after a meningoccocal outbreak versus the incidence in camps where no prophylaxis was given. The study reported a higher incidence of meningococcal disease in the comparison camps (approximate figures, 2/7,000 vs 17/9,500 over 8 weeks).[19]

Harms

Rifampin: No excess adverse effects compared with placebo were found in RCTs on throat carriage of meningococcal disease.[20,21] However, rifampin is known to turn urine and contact lenses orange and to induce hepatic microsomal enzymes, potentially rendering oral contraception ineffective. Rifampin prophylaxis may be associated with the emergence of resistant strains.[22] **Sulfadiazine:** One of 10 study participants experienced minor adverse events, including headache, dizziness, tinnitus, and nausea.[19]

Comment

RCTs addressing this question are unlikely to be performed because the intervention has few associated risks,

Table 2 *Effect of antibiotics on throat carriage: results of placebo-controlled randomized controlled trials*

Antibiotic	Group of meningococcus	Participants	Eradication Treatment, No. (%)	Eradication Placebo, No. (%)	RR (95% CI)
Rifampin (oral)[20]	B, X, Z	30 students with heavy growth on culture	11/15 (73)	2/15 (13)	5.5 (1.46-20.7)
Rifampin (oral)[21]	B, C, Y, Z29 E, W135, NT	76 airforce recruits	36/38 (95)*	3/22 (14)†	6.95 (5.77-8.12)
Minocycline (oral)[23]	Predominantly Y (63%)	149 naval recruits	37/31 (90)‡	14/48 (29)§	3.09 (2.55-3.63)
Ciprofloxacin (oral)[24]	Nongroupable (61%), B (17.5%)	120 army recruits in Finland	54/56 (97), 5 second specimens missing	7/53 (13), 6 second specimens missing or not a carrier	7.3 (6.52-8.08)
Ciprofloxacin (oral)[25]	B (41%), Z (33%)	46 health volunteers	22/23 (96)‖	2/22 (9)	10.52 (8.91-12.1)

RR = relative risk; CI = confidence interval.
*Nine lost to follow-up.
†Twenty-three either did not have meningococci before therapy or did not provide a full set of cultures.
‡Thirty-seven either did not have meningococci before therapy or did not provide a full set of cultures.
§Seven were unavailable for follow-up.
‖One did not adhere to treatment.

and meningitis has high associated risks. RCTs would also need to be large to find a difference in the incidence of meningococcal disease. In the sulfadiazine cohort study, the 2 infected people in the treatment group became infected only after leaving the camp.[19]

QUESTION: What are the effects of antibiotics in people with throat carriage of meningococcal disease?

RCTs have found that antibiotic therapy reduces throat carriage of meningococcus. We found no evidence that eradicating throat carriage reduces the risk of meningococcal disease.

Benefits

We found no systematic review. **Incidence of disease:** We found no RCTs or observational studies examining whether eradicating throat carriage of meningococcus reduces the risk of meningococcal disease. **Throat carriage:** We found 5 placebo-controlled RCTs examining the effect of antibiotics on the carriage of meningococcus in the throat (table 2).[20,21,23-25] All studies reported that antibiotics—rifampin, minocycline hydrochloride, or ciprofloxacin hydrochloride—achieved high rates of eradication (ranging from 90%-97%), except 1 trial of rifampin in students with heavy growth on culture, where the rate of eradication was 73%. Eradication rates with placebo ranged from 9% to 29%. We found 6 RCTs comparing different antibiotic regimens (table 3).[26-31] Two RCTs found no significant difference between rifampin and either minocycline, ciprofloxacin, or intramuscular ceftriax-

Table 3 *Effect of antibiotics on throat carriage: results of comparative randomized controlled trials*

Antibiotic and route	Group of meningococcus	Participants	Rate of eradication, No. (%)	RR (95% CI)*
Penicillin, IM[26]	C (49%), B (33%), NG (17%)	Adults	41/118 (35)	
Erythromycin, oral[26]	C	Adults	0/7 (0)	
Rifampin, oral[27]	B plus C (31%), NG (69%)	Adults	43/51 (84)	0.89 (0.76-1.02)
Minocycline, oral[27]	B plus C (31%), NG (69%)	Adults	36/38 (95)	
Rifampin, oral[27]	A	Children	37/48 (77)	
Sulfadimidine, oral†[28]	A	Children	0/34 (0)	
Ceftriaxone, IM[29]	A	Adults and children	66/68 (97)	1.29 (1.10-1.49)
Rifampin, oral[29]	A	Adults and children	27/36 (75)	
Ceftriaxone, IM[30]	A	Adults and children	39/41 (95)	
Ciprofloxacin, oral[30]	A	Adults and children	70/79 (89)	
Rifampin, oral[30]	A	Adults and children	85/88 (97)	
Azithromycin, oral[31]	B (63%), A (37%)	Adults	56/60 (93)	
Rifampin, oral[31]	B (63%), A (37%)	Adults	56/59 (95)	

RR = relative risk; CI = confidence interval; IM = intramuscular; NG = nongroupable.
*RR is calculated only for the 2 placebo-controlled trials. The rest are comparative trials between ≥2 regimens.
†An analogue of sulfadiazone.

one.[27,30] In a third trial, households were randomized to different treatments, and intramuscular ceftriaxone achieved higher eradication rates than rifampin.[29] Confidence in this result, however, is reduced by its weaker, cluster randomization design. In another trial, oral azithromycin proved as effective as rifampin in eradicating meningococcal throat carriage.[31]

Harms

Minocycline: In 1 RCT, adverse effects (≥1 of nausea, anorexia, dizziness, and abdominal cramps) were reported in 36% of participants.[23] **Rifampin:** See previous "Harms" section. **Ciprofloxacin:** In trials of single-dose prophylactic regimens, no more adverse effects were reported than occurred with comparison regimens or placebo.[24,25,30] Ciprofloxacin is contraindicated in pregnancy and in children because animal studies have indicated possible articular cartilage damage in developing joints.[32] **Ceftriaxone:** No significant adverse effects were encountered in the 2 trials of ceftriaxone.[29,30] In 1 trial, 12% of participants had headache.[28] Ceftriaxone is given as a single intramuscular injection. **Azithromycin:** No serious or moderate adverse effects were reported, but nausea, abdominal pain, and headache of short duration were reported equally in the azithromycin- and rifampin-treated groups.[29]

Comment

Eradication of meningococcal throat carriage is a well-accepted surrogate for preventing meningococcal disease. It is unlikely that any RCT will be conducted on the efficacy of prophylactic antibiotics in preventing secondary community-acquired meningococcal disease in household contacts because the number of participants required would be large.

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Curbside Consult

Does recreational ecstasy use cause long-term cognitive problems?

The recreational drug ecstasy, also known as "XTC" or "E," Adam, Clarity, or Essence, is widely used by young people throughout the United States and Western Europe. The drug is an amphetamine derivative, with the pharmacologic name 3,4-methylenedioxymethamphetamine (MDMA). Its popularity has been enhanced by its close association with particular forms of music and dance venues and, despite well-publicized cases of MDMA-associated death, by the widely held belief that it is a "safe" drug. Indeed, many users and social commentators believe that with better management, the negative consequences of MDMA use can be avoided.[1] This belief is based on the false premise that the danger associated with MDMA lies exclusively with poor control of environmental temperature and "bad" or adulterated drug. The latter risk, it is believed, would be eliminated by better quality control as a result of legalizing the drug. A review of the scientific literature, however, paints a very different picture of this drug, which is far from benign.

ANIMAL STUDIES

Evidence of neurotoxicity

Numerous animal studies have yielded clear evidence of potent neurotoxic effects of MDMA that are specific to central serotonergic (5-HT) systems.[2] Given the important role that 5-HT plays in regulating emotion, memory, sleep, pain, and higher order cognitive processes, it is possible that MDMA might cause a variety of behavioral and cognitive deficiencies, as well as impairing memory. Although the applicability of these results to the human condition has been vigorously contested, clinical observations are sufficient to raise legitimate concern over the negative consequences of exposure to MDMA in humans.

The evidence that MDMA is toxic to central serotonergic nerve terminals was derived from experiments in several different species, including rats[2] and a variety of subhuman primates.[3,4] The latter group appears to be up to 4 times more susceptible to MDMA than are rodents. Although initially it was thought that toxicity required multiple exposure to relatively high doses of MDMA, subsequent studies have shown that a single exposure to a high dose, or several exposures to lower doses, can induce the same profile of toxicity.[5] More recently, studies in rats showed that even a single exposure can result in some manifestations of neuronal damage[6]; in primates, both the doses and treatment regimens that produce neurotoxic effects overlap with those doses that some humans received when using ecstacy recreationally.[7]

Radiologic and cognitive changes

Despite the loss of a high proportion of 5-hydroxytryptamine (5-HT) terminals throughout the forebrain in animals, functional imaging reveals that the short- to medium-term effects of repeated MDMA treatment are largely limited to alterations in subfields of the hippocampal formation[8] where changes in glucocorticoid and 5-HT receptor expression are also evident.[9,10] These same changes in the hippocampus are thought to underlie a range of neuroendocrine, affective, and cognitive dysfunctions associated with clinical depression and normal aging. Although initially it proved difficult to find any cognitive sequelae that correlated with these changes,[11] recent animal studies have shown subtle, but lasting, deficits in cognitive behaviors that do correlate with the levels of damage to 5-HT systems in the hippocampus.[12]

HUMAN STUDIES

Evidence of neurotoxicity

Evidence from human studies has accumulated more slowly, but it is becoming apparent that the toxic effect of MDMA on central serotonergic systems found previously in animal studies has a clear parallel in human users of the drug. There is now direct evidence of a lasting decrease in 5-HT uptake sites (a marker for the integrity of 5-HT nerve terminals) in human volunteers with a past history of MDMA abuse.[13] Moreover, this decrease correlates positively with the extent of their self-reported previous exposure to the drug, and is in keeping with decreases in more general biochemical markers for central serotonergic activity reported elsewhere.[14] Positron emission tomographic (PET) imaging has revealed that the consequences of MDMA toxicity may be even more widespread than predicted from animal experiments. In addition to the hippocampal formation, both the amygdala and areas of neocortex may be affected by MDMA.[15]

Joseph Orrenzi/Trevillion Pictures

Recreational use of ecstasy can affect brain function

Cognitive changes in ecstasy users

The manifestations of this neurotoxicity, in terms of altered cerebral function and behavioral change, range from neuroendocrine impairments[16] to deficits in verbal memory and reasoning,[17] short-term memory and semantic recognition,[14] and visual memory.[18] More general indices of intelligence are also adversely affected,[19] but reports of serious long-term psychiatric disorders are still rare, with the possibility that previous exposure to MDMA merely accentuates preexisting negative personality features.[20] One particularly worrying feature that has emerged is that chronic psychosis, when manifest in MDMA users, reportedly responds poorly to therapy.[21]

The effects of MDMA on cognitive performance arising directly from drug–induced neurotoxicity may be compounded by indi-

rect effects on the cerebral circulation. As well as providing extensive innervation of forebrain neuronal systems, there is also evidence that cerebral blood vessels are innervated by the same serotonergic neurons arising from the mesencephalon.[22] It should not be surprising then that both acute and chronic treatments with MDMA produce cerebrovascular effects. In rats, the acute effect of MDMA is to produce pronounced focal cerebrovascular hyperemia,[23] which, in anatomic distribution, is directly parallel to the occurrence of MDMA-associated hemorrhagic stroke in humans.[24] In contrast, the chronic cerebrovascular effects of MDMA are more subtle under normal physiologic conditions and require the superimposition of physiologic stress before becoming fully apparent.[25] It is now evident that MDMA abuse is an important risk factor for cerebrovascular accidents in young people. If these vascular accidents are neurologically silent, however, they may only become apparent at a later date. This effect may parallel the type of cognitive decline seen in patients with multi-infarct dementia.

What should we tell ecstasy users?

Findings from animal studies suggest that long-term cognitive problems are associated with MDMA exposure, and clear parallels are now emerging from clinical experience.

It is important, however, not to overstate the case. The young people most at risk are likely to reject out of hand any "scare stories," since they feel that there have been only a few well- publicized cases of harm from the drug. These numbers are small compared to the numbers of individuals who use MDMA regularly. Studies of the drug can be criticized on the basis that they depend heavily on the quality of self-reported data. The data analysis may also be confounded by failure to report multiple drug use or inaccuracies in the reported duration of drug abstinence immediately prior to the investigation.

Nevertheless, health care professionals should be aware that cognitive disorders, mood disturbances, and increased risk of cerebrovascular accidents are among the possible long-term, negative consequences of MDMA exposure in humans.[26-28] Although subtle at first, these effects may develop into major deficits over the lifetime of an otherwise healthy individual. In particular, minor short-term deficits may be exacerbated by interaction with normal aging processes in the brain, or as a result of subsequent exposure to physiologic or psychologic stress. Even if these long-term effects are confined to a subpopulation of particularly susceptible individuals, the very scale of current usage— 3.4 million young Americans have used the drug at least once— is such that the consequences of MDMA exposure could develop into a major health care problem for the future.

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Toolbox

Ectopic pregnancy

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Ectopic pregnancy (figure 1) causes major maternal morbidity and mortality with pregnancy loss, and its incidence is increasing worldwide.[1-3] In northern Europe between 1976 and 1993, the incidence increased from 11.2 to 18.8 per 1,000 pregnancies,[2] and in 1989 the number of admissions to US hospitals for ectopic pregnancy increased from 17,800 in 1970 to 88,400.[4] These changes were greatest in women older than 35 years.[2,4] In the United Kingdom, around 11,000 cases of ectopic pregnancy occur per year (incidence, 11.5/1,000 pregnancies), with 4 deaths (a rate of 0.4/1,000 ectopic pregnancies).[1]

METHODS

We review the incidence, causes, diagnosis, and management of ectopic pregnancy. The evidence presented is from a combination of selected published articles identified from MEDLINE and a reflection of clinical practice at our institution (St James's University Hospital, Leeds, England). For the MEDLINE search, we used the term "ectopic pregnancy" combined with terms such as "incidence," "risk factors," "methotrexate," "salpingectomy," "salpingostomy," and the like.

RISK FACTORS

Although a proportion of women with ectopic pregnancy have no identifiable causal factors, the risk is increased by several factors: previous ectopic pregnancy,[5] tubal damage from infection or surgery,[6] a history of infertility,[6] therapy for in vitro fertilization,[7] increased age,[2,4] and smoking.[8]

A history of pelvic inflammatory disease is particularly important[6,9] and has been implicated in the increased incidence of ectopic pregnancy.[9,10] The risk of an ectopic pregnancy is increased 7-fold after an episode of acute salpingitis.[9] This is particularly true if the causal agent is *Chlamydia trachomatis*, which is the main cause of pelvic inflammatory disease in the United Kingdom.[11] Comprehensive programs to prevent the transmission of chlamydia decrease not only the incidence of *C trachomatis* infections but also the rate of ectopic pregnancies.[12,13]

Previous female sterilization and current use of an intrauterine contraceptive device are risk factors only when patients with ectopic pregnancy are compared with pregnant controls but not with nonpregnant women.[14,15] This is because the overall risk of pregnancy in these situations is low, but if pregnancy does occur, an ectopic pregnancy is more likely.

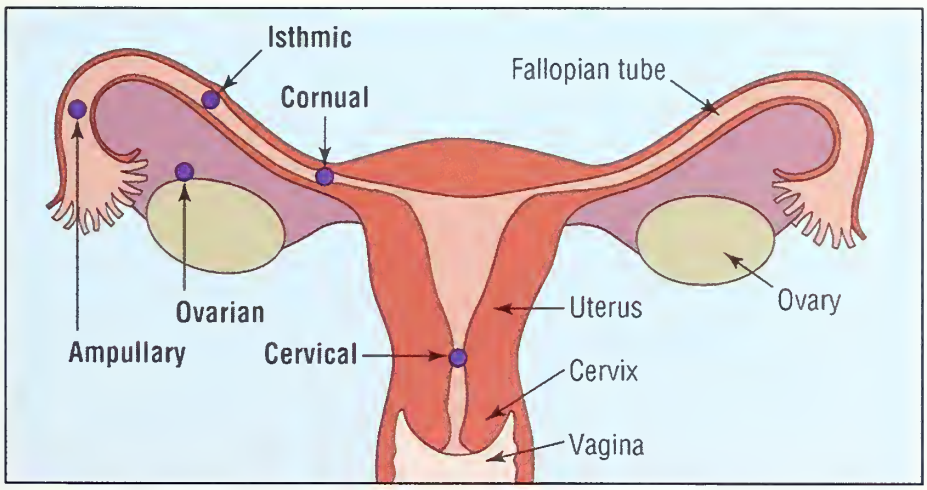

Figure 1 Sites of ectopic pregnancies

Summary points

- The incidence of ectopic pregnancy is increasing, mainly due to the increased incidence of pelvic inflammatory disease caused by *Chlamydia trachomatis*
- Ectopic pregnancy must be excluded in a sexually active woman with a positive pregnancy test, abdominal pain, and vaginal bleeding
- Early ultrasonography should be available in subsequent pregnancies for women who have had an ectopic pregnancy
- Diagnosis cannot be made clinically
- Treatment should be tailored to individual needs; in selected women, medical management can be as effective as laparoscopic salpingostomy
- Conservative surgery results in slightly higher rates of intrauterine pregnancy and a higher incidence of recurrent ectopic pregnancies

The risk of ectopic pregnancy after sterilization is only 7.3 per 1,000 within 10 years.[14]

The incidence of ectopic pregnancy after assisted reproductive techniques is 4%,[7] which is 2 to 3 times greater than the background incidence. The main risk factor in this group is tubal infertility. The incidence of heterotopic pregnancy—an ectopic pregnancy together with an intrauterine pregnancy—is also increased after assisted reproductive techniques.

PRESENTATION

Ectopic pregnancies usually present after a woman has been amenorrheic for 7 (SD 2) weeks. The diagnosis can be difficult unless the condition is suspected, and the condition can be confused with miscarriage, an ovarian accident, or pelvic inflammatory disease (see box). The abdominal pain is usually lateral. However, because as much as 9% of women report no pain and 36% lack adnexal tenderness, the history and physical examination alone do not reliably diagnose or exclude ectopic pregnancy. The presence of known risk

factors can increase suspicion, but any sexually active woman presenting with abdominal pain and vaginal bleeding after an interval of amenorrhea has an ectopic pregnancy until proved otherwise. Women who present in a collapsed state usually have had prodromal symptoms that have been overlooked. Tubal rupture is rarely sudden because it is due to invasion by the trophoblast (figure 2). Therefore, if ectopic pregnancy is at all possible, hospital referral for investigation is mandatory.

HOSPITAL DIAGNOSIS

Referral should preferably be to a consultant or center dedicated to managing problems early in pregnancy because this allows ease of investigation and continuity of outpatient care. The initial investigations are a sensitive pregnancy test and ultrasonography. The presence of an intrauterine pregnancy generally excludes ectopic pregnancy, although other ultrasonographic findings have to be considered, especially if symptoms are atypical, severe, or persistent. The use of quantitative measurement of serum concentrations of β human chorionic gonadotropin (hCG), together with transvaginal ultrasonography, has improved the diagnosis.[16] Controversy exists, however, about the concentration of serum hCG that is diagnostic.[17,18] In the presence of an ectopic mass or fluid in the pouch of Douglas, a cutoff point for a serum concentration of hCG of 1,500 IU/L is recommended, but in the absence of any ultrasonographic signs, the higher concentration of 2,000 IU/L should be the cutoff point before an ectopic pregnancy is diagnosed.[18] Ectopic pregnancies produce lower concentrations of hCG than normal pregnancies, but the change in concentrations provides more information.[19,20] In a normal pregnancy, serum concentrations of hCG double every 2 to 3.5 days in the 4th to 8th week of gestation, reaching a peak around the 8th to 12th week, as calculated from the last menstrual period (figure 3).[20,21] A failure of this increase suggests an ectopic pregnancy, although it is also associated with early pregnancy failure. A 2-day sampling interval has been recommended if paired serum specimens are being tested.[19] The accurate diagnosis of ectopic pregnancy can be lifesaving, reduces the need for invasive investigations, and allows conservative treatment.

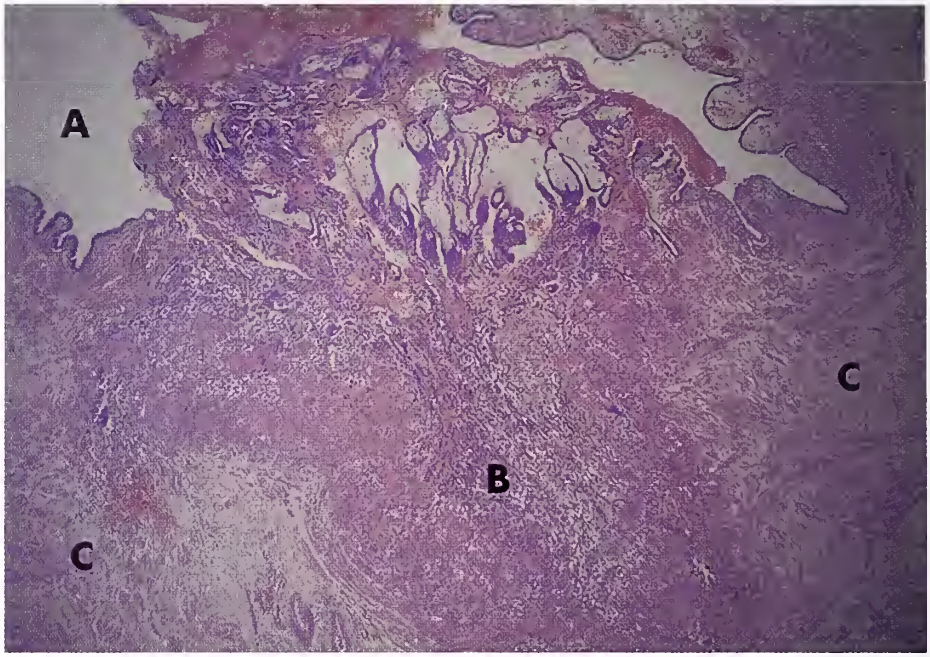

Figure 2 Trophoblast invading wall of fallopian tube, showing tubal lumen (A), trophoblast (B), and tubal wall (C) (original magnification ×25).

Presenting signs with ectopic pregnancy and percentage occurrence of history

Abdominal pain	97%
Vaginal bleeding	79%
Abdominal tenderness	91%
Adnexal tenderness	54%
History of infertility	15%
Use of an intrauterine contraceptive device	14%
Previous ectopic pregnancy	11%

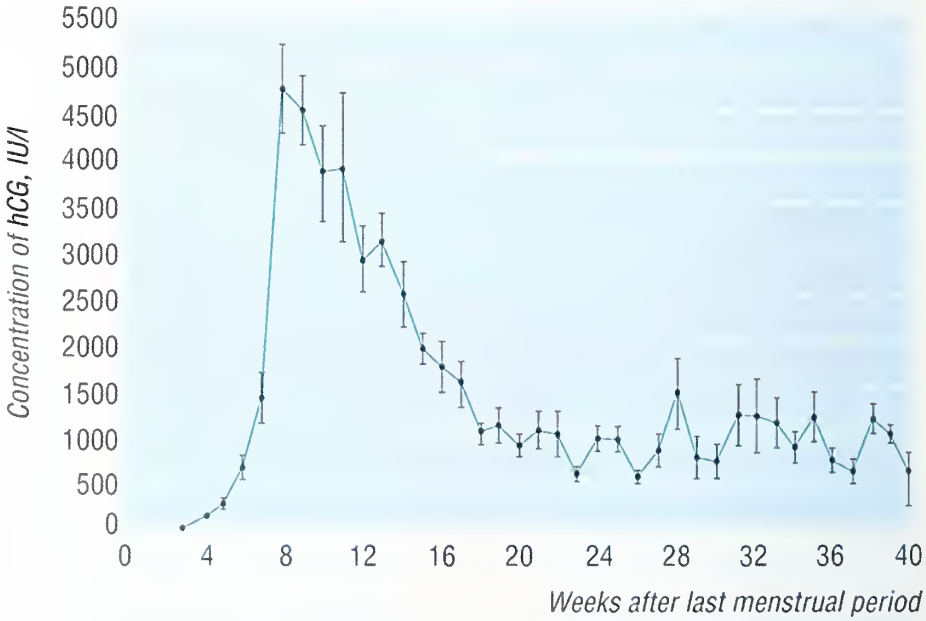

Figure 3 Mean (±SE [bars]) serum concentrations of human chorionic gonadotropin (hCG) levels in normal pregnancy (modified from Braunstein et al[21]).

Figure 4 Unruptured tube with ectopic pregnancy, showing the fimbrial end (A), and the cornual end (B).

TREATMENT

Expectant and medical management are possible and should be considered in selected cases, but it is not widely practiced in the United Kingdom. Surgery remains the mainstay of treatment, possibly resulting in many women being overtreated.

Expectant

Some ectopic pregnancies resolve spontaneously, and expectant management is possible in selected women. This is not related to the size of the ectopic pregnancy on an ultrasonogram[22,23] but the initial serum titer of hCG, and the trend in titers is an independent predictor of success.[24] Therefore, serial serum titers of hCG should be monitored in patients who are being managed expectantly. The higher the serum concentration, the more likely expectant management will fail.[22,24] Overall, if the initial serum concentration of hCG is less than 1,000 IU/L, expectant management is successful in as much as 88% of patients.[24]

MEDICAL

Methotrexate, a folic acid antagonist, is used for medical management in patients before rupture who are hemodynamically stable (figure 4).[25] It can be given intramuscularly or injected into the ectopic pregnancy sac, a route that delivers high concentrations locally with smaller systemic distribution. However, rates of successful treatment are lower than with parenterally administered methotrexate, and it requires a laparoscopic or ultrasound-guided needle procedure. Methotrexate in a single dose is more convenient than the variable-dose regimen but may carry a higher risk of persistent ectopic pregnancy.[5] Close follow-up with serial measurements of serum concentrations of hCG is required. A second course of treatment may be necessary, and some patients may require surgical intervention. Methotrexate treatment may produce substantial side effects.

Surgical

Surgical treatments may be radical (salpingectomy) or conservative (usually salpingostomy), and they may be performed by laparoscopy or laparotomy. Salpingectomy is the treatment of choice if the fallopian tube is extensively diseased or damaged because the risk of ectopic pregnancy recurring in that tube is high.

Generally, hospital stay (1.3 days) and convalescence (2.4 weeks) are shorter after laparoscopy than after laparotomy (3.1 days and 4.6 weeks, respectively).[26,27] Both techniques produce similar rates of complications and persistent trophoblast.[27,28] If persistent trophoblast is a risk, follow-up with serial measurements of serum concentrations of hCG is necessary. Because no single postoperative concentration of hCG is predictive, follow-up is necessary until complete resolution.[25] The need for a second laparoscopy should be based on symptoms rather than changes in concentrations of hCG.[26-28] In a randomized controlled trial, methotrexate and laparoscopic salpingostomy were equally effective.[29]

COST OF TREATMENT

The cost of salpingostomy is slightly more than of salpingectomy in the short term.[30] Both treatments are equally effective initially, but additional treatment for persistent ectopic pregnancies is occasionally required after salpingostomy. Although calculating the cost of an acute episode is comparatively simple, calculating the long-term costs of subsequent infertility treatment and treatment of recurrent ectopic pregnancy is more difficult.

The psychological cost is often overlooked because it is not generally viewed in the same way as other pregnancy loss. Women seem to have similar grief reactions as those with miscarriages but have the additional trauma of possibly reduced fertility. Support networks such as the Miscarriage Association are recommended to women after miscarriage, but until recently, no specific support group has been available for women after ectopic pregnancy. A support group in the United States can be found at www.ectopicpregnancy.com.

FERTILITY AFTER TREATMENT

The rates of intrauterine pregnancy after expectant management are comparable to those achieved after medical or surgical management, varying between 80% and 88%,[31,32] and rates for recurrent ectopic pregnancy vary between 4.2% and 5%.

A population-based cohort study reported a pregnancy rate of 66% regardless of whether treatment was surgical or medical.[33] Of those who conceived, 90% achieved an intrauterine pregnancy and 10% had recurrent ectopic pregnancy. The risk factors for recurrent ectopic pregnancy are previous spontaneous miscarriage, tubal damage, and age older than 30 years.[25] After treatment with methotrexate, between 62% and 70% of women had a subsequent intrauterine pregnancy, and around 8% had recurrent ectopic pregnancy.[23,25]

When comparing conservative and radical surgery, the results are conflicting, with pregnancy rates varying from no significant difference[34] to lower rates of both intrauterine pregnancy and recurrent ectopic pregnancy after salpingectomy.[23,35,36]

Irrespective of type of tubal surgery, laparoscopic treatment resulted in a higher rate of intrauterine pregnancy (77% vs 66%)[35] and a lower rate of recurrent ectopic pregnancy (7% vs 17%)[27] compared with laparotomy. A history of infertility is, however, an important factor, with an overall conception rate of 77% for all methods of surgical treatment and a rate of recurrent ectopic pregnancy of around 10%.

Despite tubal preservation in around 90% of patients and patency in 55% to 59%, neither parenteral treatment with methotrexate nor laparoscopic salpingostomy improved subsequent pregnancy performance.[29] Treatment should, therefore, be directed at therapeutic need and the wishes of the patient.

CONCLUSION

Because ectopic pregnancy cannot be diagnosed in the community, all sexually active women with a history of lower abdominal pain and vaginal bleeding should be referred to a hospital early for ultrasonography and, if necessary, measurement of serum concentrations of hCG. Women with a history of ectopic pregnancy should have early ultrasonography to verify a viable intrauterine pregnancy in their subsequent pregnancies. Diagnostic laparoscopy is necessary if the clinical situation cannot be clarified or if the patient's condition deteriorates.

Expectant and medical management of ectopic pregnancy are effective options in selected women as long as adequate facilities for monitoring are available. If surgery is necessary, the laparoscopic route results in a shorter hospital stay, but salpingostomy has no clear advantage over salpingectomy. The decision should, therefore, be made on an individual basis. Methotrexate and laparoscopic salpingostomy are equally successful in treating ectopic pregnancy.[36] Ectopic pregnancy can be prevented by decreasing the incidence of pelvic inflammatory disease and *C trachomatis* infections and improving their treatment.

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Culture and Medicine

Dental injuries due to African traditional therapies for diarrhea

The number of immigrants and refugees from Asia and Africa to developed countries has increased in the past 20 years. Through caring for these patients, western physicians have become increasingly aware of traditional healing practices such as coining, cupping, and herbal therapies.[1] Most physicians know little about traditional healing practices involving the mouth. We present 3 cases of dental malformations from care provided by traditional healers in East Africa (figures 1, 2, and 3).

REPORT OF CASES

The history in all 3 of the children indicated that traditional healers in Somalia had treated them when they were infants for the prevention or treatment of diarrhea. Patient 1's gums were cut into and the lower cuspids (the pointed teeth lateral to the 4 incisors) were extracted to prevent diarrhea. Patient 2 had a hot nail pressed into his gums in the area of the lower cuspids as treatment of an episode of gastroenteritis. The mother of both of these children also had absence of her permanent lower cuspids. Patient 3's mother reported that when he was between 4 and 6 months of age, a traditional healer made cuts in the area of the child's lower cuspids and removed gum tissue to prevent diarrhea. A Panorex film revealed absence of the right lower cuspid and the presence of a radiopaque mass, consistent with odontoma in that site. A deformed and impacted left lower cuspid with associated radiopaque structures was identified in the left mandible. An exploration was done and a biopsy specimen taken of these structures. Biopsy findings were consistent with an odontoma (a benign tumor) in the mandible at the expected site of the deformed permanent cuspid tooth bud on the right side. On the left side, an impacted and deformed permanent cuspid developed. Oral surgeons speculated that the odontoma formed as a result of the disruption of the dental tissues resulting from the traditional treatment. Both mothers reported that this was a common procedure in some regions of Somalia.

Figure 1 On a routine physical examination, this 6-year-old Somali boy, a recent immigrant to the United States, was noted to be missing both primary lower cuspids.

Figure 2 A 7-year-old Somali boy (brother of boy in figure 1) was also noted on a routine physical examination to have enamel defects located centrally on the buccal surface of both lower cuspids. The right cuspid was broken off above the defect.

EXTENT OF PRACTICE

Reports of traditional healing practices of many African countries in which the cuspids and incisors were removed or mutilated have been numerous: 1% to 60% in certain villages in Tanzania,[2,3] 16% in northern Uganda,[4] 22% among urban children in Sudan,[5] 59% among Ethiopian Jews,[6] 70% in some populations in Ethiopia,[7] 87% among the Maasai in Kenya,[8] and 100% among infants younger than 18 months admitted to a hospital in southern Sudan.[9] We were unable to find any reports of the practice among Somali populations.

All reports indicate that there are strong cultural beliefs that the swelling in the area of the gums associated with the unerupted cuspids is a cause of persistent fever and diarrhea. A traditional healer is consulted to remove or lance this area of the gums. In most instances, the lower cuspids are extracted bilaterally, but the extracting of up-

Figure 3 A 16-year-old Somali boy, who had been in the United States for several years, was noted by his primary care dentist to be missing both permanent lower incisors.

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per cuspids and lower incisors has also been reported. Lancing of the unerupted cuspids with a hot needle has been reported in the Sudan and has been associated with enamel defects on the buccal surface of the lower cuspids.[7] Instruments used for these procedures include penknives, metal blades made from spoon handles or bike tire spokes, and sharp fingernails. In some cultures, salt or herbs are applied to the area of the gum that is injured following the procedure.[2,5,10]

The procedure is carried out by a traditional healer. In some cultures, the healer is a respected older woman.[2] In others, it is a person, usually a man, who makes a living from this specific practice.[11] The instruments used are often not sterilized, and no topical anesthesia is used. The procedure is performed to prevent or treat gastroenteritis and prolonged fever. One study from Tanzania[5] in which parents were interviewed about the health behaviors that had occurred before the traditional treatment showed that parents often consulted a traditional healer after 1 or more visits to a government health facility. They resorted to the traditional treatment because their child's symptoms persisted despite evaluation and receiving medication from a local hospital. The age at which the extractions and lancing occurred varied from as early as 1 month to 2 to 3 years. Peak ages for the procedure in most studies were between 4 and 18 months.[2-5,7,8,11]

CONSEQUENCE OF CUSPID DISRUPTION

Dental abnormalities are the primary consequence of the practice. In addition to enamel defects and loss of teeth, the mandibular arch size has been documented to be smaller in those who have had the extractions.[12] Partial extraction of the cuspids often results in hypoplasia of adjacent primary and permanent teeth. The retention of primary lateral incisors with distal eruption of permanent successors has also been noted, along with displacement and impaction of the permanent cuspid.[4,9,10] The practice of removing or disrupting the primary cuspid tooth typically occurs before the eruption of the cuspid. The procedure is considered a success if the "tooth worm" is removed along with the primary cuspid. The tooth worm is the dental lamina, the permanent cuspid before crown development. If the dental lamina is not removed, it may continue to develop normally, although it is more likely damaged, resulting in a dysplastic or maldeveloped permanent tooth.

Andreasen and Ravin list 10 possible outcomes of trauma to a primary tooth, including "odontoma-like malformation."[13] A true odontoma might result from the extraction of an unerupted cuspid, with concurrent damage to the dental lamina. A case of a small odontoma at the site of a mandibular canine extracted early in childhood by a traditional healer was recently reported in an Ethiopian teenager who now resides in Sweden.[14] More cases may be seen as these immigrant children receive dental care in developed countries.

The practice has other consequences. Infection at the site of the procedure and death from sepsis have been documented in a number of studies. Of 124 infants who had the procedure in Tanzania, 10 died of infectious complications.[15] In 1 birth cohort in Ethiopia of 594 children who had the procedure and were observed for a year, 1 child died.[16] The child had undergone a dual procedure involving uvulectomy and dental extraction, and the maternal history suggested that the child died of infectious complications. Why the mortality rate is so low is unclear, given that the instruments that are used are not routinely sterilized. Physicians working in Africa report that traditional practitioners will do the procedure on several successive children in a short period of time using the same instrument. This practice is common in areas of Kenya, where nearly a third of the pregnant women are documented to be positive for the human immunodeficiency virus, suggesting a possible mechanism for the horizontal spread of the virus (Juliana Otieno, MD, International Fellow, New Nyanza Provincial Hospital, Kenya; oral communication; April 1999).

An Ethiopian study showed decreased growth in children who had dental extractions as long as 4 months after the extractions, and this reduction was observed even when controlling for illness episodes.[16] Perhaps the most important consequence of this practice is that the children are not correctly diagnosed or treated for their febrile or gastrointestinal illnesses because parents either do not return to western facilities or seek care directly from a traditional healer.

Public health interventions have been attempted to modify the adverse effects of this practice. In the early 1980s, a health campaign was carried out in Tanzania urging people not to do the procedure, and it was outlawed. A survey in 1992, however, indicated that the procedure was still prevalent in many regions of the country.[5] In some areas, the practice has changed from these harmful extractions to rubbing medicinal herbs on the gums. In Kenya, attempts have been made to train traditional practitioners to recognize signs of dehydration and sepsis in children and to provide them with oral rehydration solution (J Otieno, oral communication, April 1999). There have been no reports on the outcome of these public health efforts. Parents we have spoken with from Somalia indicate that the procedure is a source of income for the traditional healers and has become deeply ingrained in the society because of the strong folk belief in its efficacy.

HISTORY OF PROCEDURE

The historical origins of the procedure are not clear. Several authors and our conversations with local East African health outreach workers suggest that this procedure is relatively new in Africa. The first reports of the procedure were from the 1930s and were described in the Nuer tribe in Africa. In Kenya, the procedure was thought to have started among the Maasai in the 1960s and to have spread from neighboring Uganda and Tanzania.[2] In southern Sudan, the practice is thought to have been brought in by refugees from neighboring countries.[7] Our adult dental clinic rarely sees absent cuspids in East African older

adults, which suggests that the practice has been prevalent among our refugee population only for the past 30 to 40 years.

Incising the gum over an erupting tooth was promoted in Europe as early as 1742 by Joseph Hurlock as a means of decreasing pain associated with eruption.[17] The practice was continued into this century in Europe and the United States and may have been used by colonial dentists in East Africa and adopted by traditional healers to treat fever and diarrhea.

Virtually all cultures have specific beliefs associating common childhood illnesses with tooth eruption.[18-21] Given the high morbidity and mortality associated with childhood gastroenteritis and febrile conditions in developing countries, it is not surprising that parents associate these illnesses with teething and subject their children to traumatic procedures in the hope of preventing and treating such feared conditions. Educating parents and traditional healers and instituting public health measures to provide clean water supplies and sanitation are needed before these harmful traditional healing practices will cease.

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COMMENTARY

Is teething associated with diarrhea?

The common perception among dentists is that teething in babies and children may be accompanied by increased drooling, a slight rise in temperature, and perhaps increased irritability, but these symptoms are relatively minor. Teething and diarrhea are not usually associated. The article by Graham and colleagues reminds us that although this relatively benign view of teething-related discomfort is held by much of the western world, other cultures may hold very different views.

As the authors mention, lancing the gums overlying erupting primary teeth was a common procedure in Europe and the United States in the late 19th and early 20th centuries. They discuss a variation on this practice in which lancing and possible tooth extraction are limited to the area of the primary canines. Perhaps some cultures perceive the eruption of the canines to cause more symptoms than the eruption of other teeth. The practice of lancing the gums overlying the primary canines or extracting the unerupted teeth is certainly of concern. These practices can lead to altered esthetics and spacing in the permanent dentition, as well as trauma to the infant. As the authors indicate, the use of nonsterile techniques may cause increased morbidity and even mortality.

The fact that some women believe that their child's diarrhea is due to tooth eruption is of concern to primary care professionals. In studies conducted in Florida[1] and in western Africa,[2] parents tended to view the diarrhea as less serious when they thought it was due to teething. But children with "teething diarrhea" are just as likely to develop dehydration as children with nonteething diarrhea. Primary care providers should be aware of these various beliefs regarding the relationship between infant diarrhea and teething. They should educate parents to recognize early signs of dehydration and should discourage the belief that teething causes diarrhea.

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Medical Myth

Heparin should be administered to every patient admitted to the hospital with possible unstable angina

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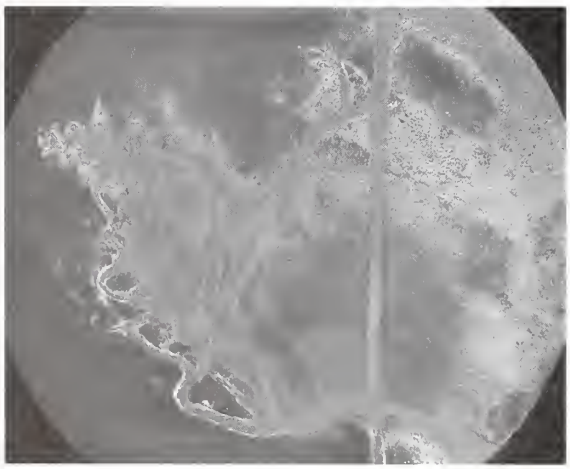
It is routine in many practice settings to administer heparin to all patients admitted with the diagnosis of unstable angina. The idea that heparin is effective in the treatment of all patients with this disorder is a potentially dangerous myth.

Each year in the United States, 5 million patients present to emergency departments with chest pain. One million of these patients are given a working diagnosis of unstable angina.[1] However, many prove not to have the disease. Even in patients with proven unstable angina, there is a wide spectrum of risk for adverse outcomes. Patients admitted with this diagnosis should be risk stratified into low, intermediate, and high risk for death, myocardial infarction (MI), and other complications.[2,3] Risk stratification reduces the possibility of giving heparin, a potentially dangerous therapy, to low-risk patients who receive little or no benefit from this drug.

ESSENTIAL ROLE OF ASPIRIN IN UNSTABLE ANGINA

To understand the utility of heparin in unstable angina, clinicians should first understand the essential role of aspirin in acute coronary syndromes. Aspirin remains the most effective agent in the treatment of these syndromes. In patients with unstable angina, its use is associated with a relative reduction in the incidence of MI of as much as 50% (number needed to treat [NNT] = 20)[4,5] and a relative reduction in mortality of 23% (NNT = 40).[6] Aspirin lacks major side effects and has few contraindications. It can, therefore, be given to nearly all patients with unstable angina. Even those patients ultimately proved to be free of unstable angina are not placed at excessive risk from this therapy. The number needed to harm is high enough to warrant giving aspirin therapy to all patients with possible unstable angina.



CNRI/SPL

Heparin is not for all patients with unstable angina.

CLINICAL EFFICACY OF HEPARIN

Heparin has been advocated as additional therapy for unstable angina. The theoretic benefit of adding heparin is that it may prevent the propagation of an established thrombus, allowing time for endogenous fibrinolysis to occur. The drug presumably should act synergistically with the antiplatelet effects of aspirin to reduce coronary artery obstruction and ischemia, ultimately lessening morbidity and mortality.[7]

In a meta-analysis to assess the clinical efficacy of heparin in unstable angina, Oler and colleagues found only 6 randomized studies (1,353 patients) since 1966 of the use of heparin with aspirin for unstable angina.[7] Each trial showed a trend suggesting benefit from the dual therapy, but none showed a statistically significant reduction in MI and death during heparin infusion. When these studies were combined in the meta-analysis, the authors found an absolute reduction in the incidence of MI and death of 2.4% from combined therapy, which was not significant ($P = 0.06$). The NNT to prevent 1 case of MI or death was 40. By 12 weeks, there was no reduction at all in the incidence of MI or death. In other words, the nonsignificant trend toward a reduction in MI and death was sustained only in patients while the heparin was being infused and for a short time after.

Five of the 6 trials in the meta-analysis included patients who would be risk stratified as being at intermediate to high risk of having unstable angina. The characteristics of these acutely ill patients included a history of MI, electrocardiographic changes, abnormal findings on an exercise treadmill test, and a history suggestive of unstable angina. In patients admitted with this diagnosis who have no disease or low-risk disease, the NNT to prevent MI or death is certainly much greater than 40.

HAZARDS OF HEPARIN THERAPY

Heparin is a potentially harmful therapy with a narrow therapeutic window. It is the number 1 cause of drug-related deaths in the inpatient setting.[8] The administration of unfractionated heparin places patients at risk of

bleeding by altering blood coagulation, increasing vascular permeability, and inhibiting platelet function.[9(p1168)] In the meta-analysis by Oler and associates, the absolute increase in the risk of major bleeding from dual therapy compared with giving aspirin alone was 1.1%.[7] This correlates with a number needed to harm of 90. In other words, even excluding patients who have contraindications to heparin, for every 90 patients given heparin, 1 will have major bleeding. Furthermore, for every 34 patients treated, 1 will develop some form of heparin-induced thrombocytopenia after 3 to 5 days of therapy.[10]

Hence, the risk-benefit ratio for heparin, unlike aspirin, is acceptable only in our intermediate- to high-risk patients who have no contraindications. Even in the high-risk group, patients appear to benefit only during heparin infusion. One hypothesis is that heparin may further lessen morbidity and mortality in patients with unstable angina by bridging the gap between admission and definitive revascularization procedures like angioplasty, stenting, and coronary artery bypass grafting. To date, this hypothesis is unproven.

ROLE OF LOW-MOLECULAR-WEIGHT HEPARIN

Low-molecular-weight (LMW) heparin, such as enoxaparin, has been advocated as a replacement for unfractionated heparin for use in patients with acute coronary artery syndromes. It has several advantages. First, it is easier to use than standard intravenous heparin because it is subcutaneously administered, needs only twice-a-day dosing, and the partial thromboplastin time does not need monitoring.[11] Second, whereas enoxaparin and standard heparin are associated with the same incidence of major bleeding episodes,[12] LMW heparin has a lower incidence of heparin-induced thrombocytopenia.[13] Therefore, we can assume that it is at least as safe as unfractionated heparin. Third, although LMW heparin costs more per vial than regular heparin, when total therapy costs are considered, LMW heparin costs the same as standard heparin.[14]

The efficacy of LMW heparin has been compared with that of unfractionated heparin in patients with unstable angina. Again, all studies included acutely ill patients classified as having intermediate- to high-risk disease. The randomized controlled Efficacy and Safety of Subcutaneous Enoxaparin in Non-Q-Wave Coronary Events trial (n = 3,171) compared the use of aspirin plus enoxaparin with that of aspirin plus unfractionated heparin.[12] There was a 3.2% absolute reduction ($P = 0.02$) in the primary end points of recurrent angina, MI, and death at 14 days (NNT = 30). This benefit appeared to be sustained at 30 days, despite maximum therapy for only 8 days. When only MI and death were evaluated at 14 and 30 days, there was no significant reduction in the incidence of MI or death. More recently, in the Thrombolysis in Myocardial Infarction (TIMI) 11B trial (n = 3,910), the use of enoxaparin was compared with that of unfractionated heparin in high-risk patients with unstable angina, non–Q-wave MI, or both.[15] There was no significant difference in outcomes when the incidences of MI and death were measured at 8 days (4.6% vs 5.9% [enoxaparin vs unfractionated heparin]; $P = 0.07$), 14 days (5.7% vs 6.9%; $P = 0.11$), and 43 days (7.9% vs 8.9%; $P = 0.28$) Enoxaparin appears to be at least as efficacious as unfractionated heparin and is possibly safer, but its use still should be considered only in intermediate- to high-risk patients.

Enoxaparin is currently the only LMW heparin approved by the Food and Drug Administration for use in patients with unstable angina. Other LMW heparins have been compared with standard heparin, with varying results. In a study of 219 patients, there was a significant decrease in the incidence of recurrent angina and a nonsignificant trend in a reduction in MI in a group receiving aspirin and the LMW heparin nadroparin.[16] However, in the recent European study of fraxiparine use in ischemic syndrome (3,468 patients), in which the use of nadroparin was compared with unfractionated heparin, there was no significant difference between the 2 treatments in the primary outcomes of death, MI, or refractory ischemia.[17] In another study, which used the dalteparin sodium form of LMW heparin, trends were actually shown favoring the use of regular heparin.[18] The FRISC* II study looked at long-term therapy (3 months) with dalteparin for patients with unstable angina.[19] The researchers found a nonsignificant trend in the reduction of MI and death during treatment with the drug, and the trend was not sustained at 6 months, suggesting that any possible benefit of dalteparin use was lost when the drug was withdrawn.

CONCLUSIONS

Heparin, whether unfractionated or LMW, should not be given to all patients with the diagnosis of unstable angina. Each patient needs to be risk stratified. Patients with unstable angina who have low-risk disease should not be given heparin. When the patient is deemed at intermediate or high risk of MI and death, the clinician may consider the use of heparin if the patient has no contraindications. However, even in high-risk patients, heparin does not appear to have a sustained benefit, and therefore, its use in any patient with unstable angina may be questioned. Treatment with LMW heparin has some advantages over that of regular heparin.

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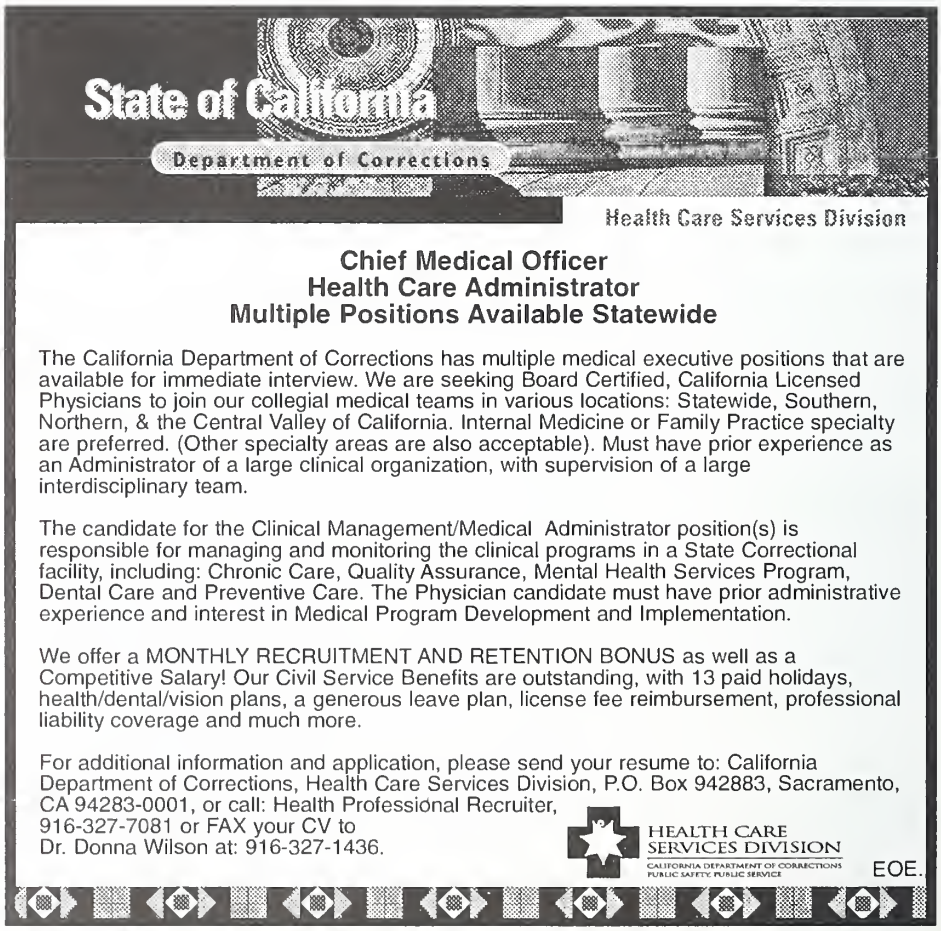

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Speaker's Corner

A little conversation: reflections of a hospital volunteer

Hospitals in general are not cherished places. Hospitals exude a cold, bleak, and awful feeling. They are easy to dislike. But, I like hospitals. They are the places where I have grown up, waited expectantly for my father to finish one of his many shifts, celebrated birthdays, and most of all, been touched by the most amazing feeling that this world has brought forth.

I do volunteer work at Cedars-Sinai Medical Center in Los Angeles, California; I aspire to be a physician someday. From a distance, the Center is an enormous group of sterile-looking buildings. On entering, there is a strangeness in the air. Even to this day, I hesitate venturing into the "inner depths" of the hospital, such as the ICUs, without the company of another soul. The never-ceasing activity of patients' monitors makes me feel as if I'm being watched. I find myself checking my backside, hoping no one is present, yet also hoping someone is. Nevertheless, this gargantuan place has become less intimidating with time. Indeed, I now find myself at peace within it. A good thing too, for soon it will be my place of work, rather, my life.

> All that they yearn for is some personal attention—a brief conversation—that will remove them from their aloneness

The people I meet as a hospital volunteer usually have a terrible illness. Some may get better, some will certainly die. In all likelihood, they are scared, and every emotion that they have ever experienced is racing inside of them. For the majority, all that they yearn for is some personal attention—a brief conversation—that will momentarily remove them from their aloneness in their downward spiraling world. People too often say, "talk is cheap." But the spoken word has no monetary value; it is materially useless. Yet, therein lies its value.

It is easy to offer a few supportive and reassuring words, words with value, to someone who is consumed with a fearful future, and possible imminent mortality. Why do we not act in this manner more often? Perhaps our own lives are too busy, and too important, to take a few minutes to ease the mind of a person in need. Or, even though we realize that death is a part of all of our lives, it still creates uneasiness to think of losing a loved one through death. It is simply easier not to become involved, not to interact.

In my experience, from the moment that I enter a patient's room and begin a conversation with them, I can feel their gloom lifting. Somehow, my talking with them allows their medical problems to temporarily vanish. The talk seems natural, as though we're on a street corner, and we were old friends being reacquainted. We are intrigued by each other. Everything around this patient and me somehow ties us together. Physically, we share the same air, space, and time during the interaction, but the gravity of the situation causes any other differences to dissipate, and the commonness of our own humanity shows through. The two of us bond, forming a special mental unity that momentarily replaces their anxiety.

Each individual patient's situation is different and cannot be recreated; however, each situation requires the same thing—a little communication. When in the presence of these patients, I feel different. The occasion allows me to venture inside each person's soul and I am uplifted to see the joy it brings to the patients. If I can ease someone's overall tensions, temporarily take their minds off the severe pain they feel, or the doom that they see ahead, I may be doing my part to make this lifetime better. Life is precious; it is momentary; it is too short.

Brian W Ault, age 17
Los Angeles, California

Letter from the Southwest

The truth about proof

Mark Carroll, Flagstaff, AZ

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I am bothered by proof. The zeal for evidence that so characterizes contemporary medicine leaves me ambivalent and unsettled. On the one hand, outcomes researchers can corral companies motivated by profit to demonstrate product effectiveness before expensive yet marginally helpful therapies are loosed upon the public. On the other hand, evidence-based academicians can focus scientific attention on some aspects of medical practice that seem more like value than experimental therapy. Does new drug A work better than old workhorse B? This question seems reasonable. Does compassion in patient care offer measurable results? This question seems more troubling.

Consider the following scenario: a woman with unremitting breast cancer reviews treatment options with her oncologist: "Bone marrow transplantation isn't effective," the doctor says. "Neither is additional surgery, chemotherapy, or radiation." "What else is left?" asks the woman. "Well," the oncologist replies, "There is psychosocial treatment. It's unproven, but I've seen it work."

Lest you think this exchange absurd, let me allay your annoyance: research supports psychosocial "treatment" of women with metastatic breast cancer. The seminal study, published more than 10 years ago,[1] shows that women who received weekly support therapy lived longer than those who did not. Relieved? I'm not. The study authors predicted that psychosocial support, although potentially beneficial for psychological well-being, would have no effect on the course of their patients' disease. They sought to debunk the business of support, rather than demonstrate its value. The improved survival data took them by surprise.

Maybe you find this divergence between expectation and outcome unproblematic. Science, you might contend, is nothing but a challenge to expectation, an objective means of assessing outcome when subjective bias and experience misguide instead of inform decision making. We need to know what we are doing, you might argue. We need to know where we are being wasteful.

Suppose, however, that the data had showed something different. Suppose the study of women with breast cancer had showed that psychosocial treatment had no effect on survival or that it had shortened survival instead of extending it. Would we feel comfortable calling psychosocial support wasteful? Would we direct physicians, nurses, and oncology practices not to offer it?

> We trade on patient data like bankers and brokers and publish research observations like uninvolved neutral parties

I recently posed this hypothetic dilemma to a panel of physicians convened to review their ongoing studies of compassion and psychosocial treatment in medicine. Some of the researchers responded with decidedly unscientific and unsympathetic alacrity. "You have to listen to the data," 1 doctor replied. "Sometimes it speaks to you in ways you aren't appreciating." Another stressed the practical importance of documenting the role that compassion plays in healing. "Third-party payers will only fund treatments with proven efficacy," he said. "Without the data, people won't get the services."

Listen to the data? Prove efficacy for third-party payers? Such jargon sounds more like political gamesmanship than dispassionate scientific study. It subverts the art of healing to the callous rules of the marketplace. It makes me wonder whether uncertainty, not suffering, has become medicine's foremost therapeutic challenge, whether statistical analysis, not compassion, has become the preferred prescription for meaningful care.

The truth about proof is that there is none. Quantum physics teaches that where we most search for certainty, we find only probability. What is observed depends on who observes and how. Physicists working in the whirling world of the subatomic particle have learned to accept such uncertainty; physicians working in the supercharged world of human frailty have not. Want to know both the speed and location of an electron? A physicist says you can't. Want to know both the cause and best treatment of a patient's illness? Doctors do it every day.

So we deceive ourselves and justify our involvement in patient care through the statistical analysis of symptoms, treatments, and clinical outcomes. Instead of treasuring the participatory and often highly personal nature of healing, physicians reject individual perspective as a threat to the institutional status quo. We press subjectivity through the tired mill of the placebo-controlled trial and distract attention from inexplicable recovery and suffering with complicated methods and analysis. We trade on patient data like bankers and brokers and publish research observations like uninvolved neutral parties. We distance those in need from those most able to help.

Proponents of evidence-based medicine can no doubt list an impressive array of useless or unsafe therapies discarded because of careful study and analysis. While I respect such achievements and contributions, I worry that increasing efforts to quantify the qualitative threaten, rather than strengthen, our basic commitment to sick people. Any day now, studies allegedly proving or disproving the effectiveness and efficiency of compassion in health care are due to be published. I, for one, won't feel comforted to see them in print.

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COMMENTARY

Subjectivity can be inhumane

Gavin Yamey, Deputy editor, *wjm*

West J Med 2000;173:143

In Carroll's postmodern world, proof is a lie, while intuition is an ally. Modernism and objectivity are inhumane, while subjectivity is the kinder, more gentle way to help the sick and suffering. And evidence-based medicine is not to be trusted. This way cruelty lies, for no amount of statistical analysis can prove how to provide compassionate care to each unique patient.

But the problem with making subjectivity our god is that it is sometimes wrong. Worse still, it is sometimes callous. Practices based on intuitive thinking have proven harmful. One example is the technique of performing episiotomies on women in labor. The rationale seemed kind: a clean cut is surely preferable to a spontaneous tear, and it is bound to protect the perineum and sphincters during childbirth. But the evidence tells a different stoty. Women who have episiotomies are at higher risk of fecal incontinence than those with spontaneous lacerations.[1] Our instincts were wrong. Medicine must always evolve, continually integrating what is "known" into our daily working lives. We must be willing to let go of our previous truths, as new truths arise. Doctors are being unkind to their patients when they place their faith in instinct and tradition alone.

Evidence is only tyrannical when it is applied in a vacuum. The art of caring for the sick involves adapting the best available clinical evidence to the individual patient. Evidence-based medicine has the individual as its focus, emphasizing the "compassionate use of individual patients' predicaments, rights, and preferences in making clinical decisions about their care."[2] This emphasis is not so far from postmodernism's view of a unique, lived experience.[3]

Sometimes evidence is, of course, unnecessary. We don't need a randomized controlled trial to know it is valuable to hold the hand of the dying: patients tell us that they find it comforting, and we see how it eases their fear and isolation. There are many such values in health care that are based on justice and equanimity. The charity Age Concern has outlined 12 principles of "a good death." These include affording patients dignity, allowing them access to spiritual and emotional support, and ensuring that they are able to retain control over what remains of their lives.[4] We don't need to prove the value of these just and ethically sound principles.

And sometimes, when we search for evidence, we find none of any worth. Many systematic reviews show that the original trials were of such poor quality that no useful conclusions can be drawn. Does this mean that we should abandon such literature reviews? I would argue not, for these unanswered questions can become a compassionate guide, telling us which areas of clinical medicine we have neglected in our research efforts.

Carroll reminds us how dangerous it can be to put our trust in evidence. He is right, of course, because there is no underlying, objective reality that can explain all of medicine's uncertainties. Proof is sometimes used in a vain attempt to capture and control knowledge. More worrying is the question of who "owns" the evidence, and whose interests does it promote? The pharmaceutical industry, for example, funds many of the highest profile trials, and it has attempted to suppress negative trial results.[5] There is an ancient Arabic saying, which is: "Trust in God, but tie up your camel at night." We should use evidence to guide us in our clinical practice, but we must always be wary of its origins.

But if the truth about proof is really that there is none at all, then what should we tell our patients when they ask us which is the best treatment? We could answer them by quoting an early postmodernist, Benjamin Franklin, who said: "He's the best physician that knows the worthlessness of most medicines."[6] This therapeutic nihilism, however, would be an unkind lie. Evidence-based medicine is not perfect, but in giving patients the best available information about benefits and harms, it is the most humane we have to offer.

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capsule

Television promotes unsafe behaviors US television networks such as Nickelodeon, Cartoon Network, and Fox bombard children with unsafe messages (*Arch Pediatr Adolesc Med* 2000;154:366-369). In a content analysis, over half of their programs for children depicted unsafe, unchallenged behaviors such as running across a road without looking or riding a bicycle without a helmet. Public service broadcasters did slightly better.

The breast-feeding dilemma

David Heiden

Mother and baby. Wad Sherrife refugee camp, Eastern Sudan, 1987

When I worked in a refugee camp on the Cambodian border in the spring of 1980, we encouraged breast-feeding as an important measure to reduce infant mortality. We regarded Nestlé Corporation, then the most aggressive peddler of infant formula in developing countries, as the devil incarnate. We circulated information sheets denouncing Nestlé, and we posted signs all over camp and our ward that baby bottles were forbidden.

One day, I caught a woman bottle-feeding her infant on our ward. Later, when I continued my rounds, I notice her still in tears, and I learned that she had tried to breast-feed but hadn't any milk. She had spent a small fortune with a Krou Khymer, a traditional healer, trying different herbs, and then went to the black market and spent more money buying western medicines. She'd tried quinine, penicillin, and chloramphenicol, all without success.

I regret harshly chastising her, but there were good reasons for us to encourage breast- over bottle-feeding. There was often no clean water to mix formula and no refrigeration to prevent the formula from turning bad. Formula offered lower quality nutrition compared to breast milk and none of its antibodies. Bottles were also expensive.

But now, there is an HIV epidemic. In some countries of sub-Saharan Africa, up to 20% of women of childbearing age are infected. Breast-feeding may carry a death sentence by transmitting HIV from mother to child.

David Heiden is an opthalmologist practicing in San Francisco

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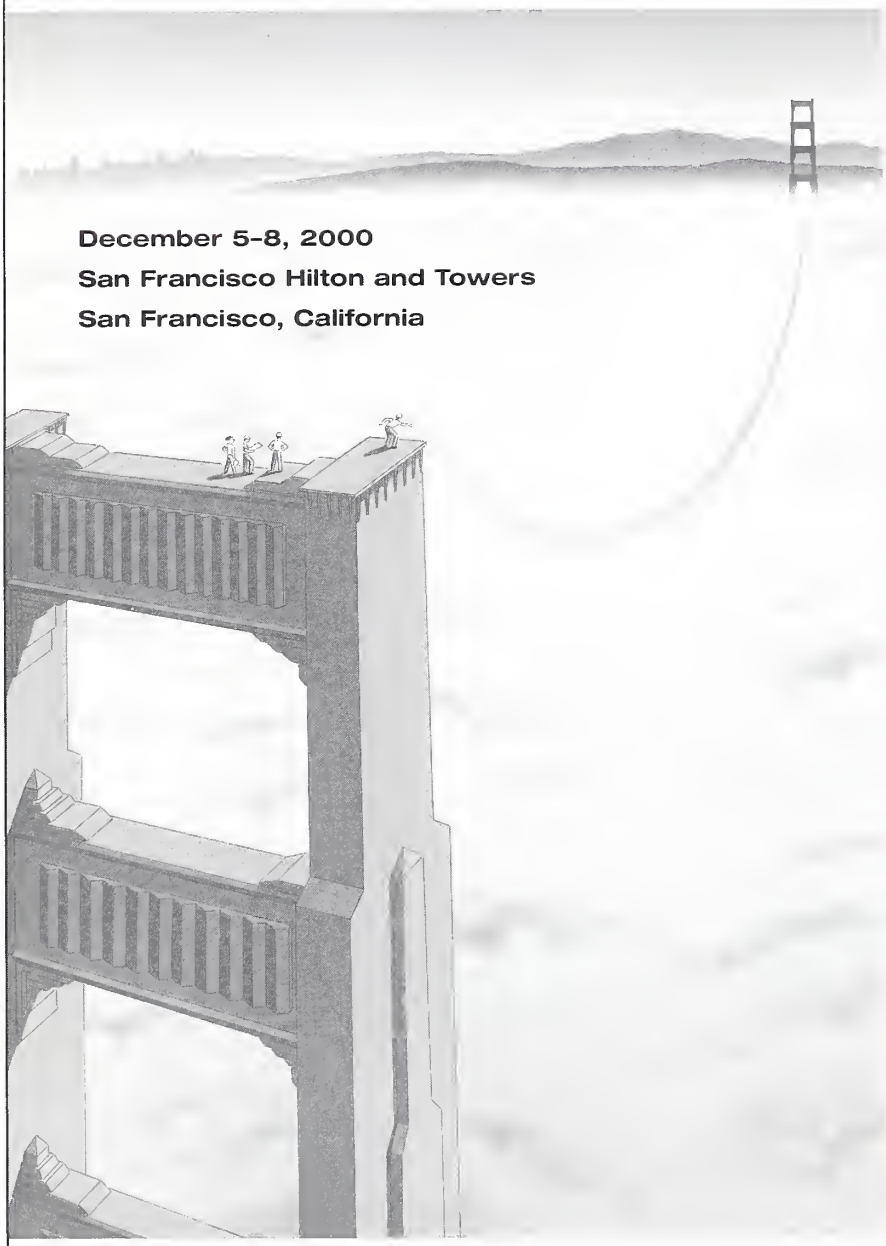

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This month in wjm

American films show intentional violence

The American action movie is a notoriously violent genre, but violence has now crept into other types of movies, even cartoons and comedies. Public health professionals are concerned about its possible social effects. McArthur and colleagues analyzed depictions of violence in the top 100 grossing American films of 1994 and found a median number of 16 (p 164). The physical consequences of violence are rarely shown in films. But in a commentary on p 169, Guyer asks, "Does the absence of blood and gore really make the violence less convincing?"

Doctors and patients report satisfaction with telemedicine

New technologies bring new hopes of panaceas, so the hype that surrounds telemedicine is easy to understand. Primary care physicians stand to gain from this medical innovation, because it may improve their communication with distant specialists. Nesbitt and colleagues reviewed 1,000 consecutive telemedicine consultations in the UC Davis Telemedicine Program (p 169) and found that physicians and patients reported high levels of satisfaction. But doctor-patient consultations are complex, says Whitten on p 174, and they cannot be understood merely by using satisfaction questionnaires.

US women have limited reproductive health rights

US law theoretically supports a woman's right to make reproductive choices. But a woman who chooses to terminate a pregnancy has many barriers in her way, says McCarthy in an Op-Ed on p 151. In most counties, there is no doctor to perform an abortion, whereas only 14% of US hospitals permit abortions to be performed at the facility. McCarthy outlines ways in which primary care physicians can help to reverse this marginalization of reproductive health care.

A new code of medical ethics is needed

The health care environment is constantly changing, bringing new ethical dilemmas. Traditional medical ethics, based on a 19th century American Medical Association code, fail to address the modern duties of the physician—such as providing universal access to health care and preventive services. Charles and colleagues outline a new ethical framework and show how it can be applied to ethically complex cases (p 198).

The treatment of acute, severe migraine

Migraine headache is a disabling condition associated with other unpleasant symptoms, such as nausea, vomiting, and photophobia. Most episodes can be managed in the community, but a few patients require treatment in the emergency department. On p 189, Kelly reviews the evidence on the efficacy and safety of emergency migraine therapies. She concludes that three agents are particularly effective.

Editor's pick

We cannot turn the page of a magazine, drive along the highway, or listen to the radio or TV without being bombarded by the commercial media. Not only are there people constantly trying to sell us products, but also there are groups promoting their test, their disease, or their way of thinking. Robinson and Hoffman take different sides of such a medical debate (p 148). On the one side are the devotees of a quick intervention that relies on high-tech clot busters to open access to ischemic areas of the brain. On the other are the skeptical scholars who want convincing proof not only of local effect but also of measurable meaningful outcomes. Although both authors have no competing interests to declare, the debate outside of these pages is not evenly balanced. One side has millions of drug industry dollars to promote its view. The other has no funding and just the conviction and dedication of a few critics.

Gillon writes on p 206 about the "white coat ceremony"—a rite of passage intended to remind beginning medical students of the profession's dedication to people rather than to diseases. This ceremony, now a ritual at many American medical schools, is also a promotion—this time of a foundation based in New York City. It seems honest and noble enough, but it is clearly intended to influence thinking and promote one point of view.

Perhaps the public's greatest insight into the medical profession comes from their weekly viewing of the TV drama *ER*. Even in our medical school classes, *ER* episodes prompt a full day of discussion and debate. While clearly produced as "entertainment," its executive producer Neal Baer argues that it is also a socially responsible vehicle for promoting public health ideas (p 157). *ER* may have done more to influence the American public's attitudes on such topics as domestic violence, rape, child abuse, and mental health than have scores of well-meaning public health pamphlets, public service spots, and campaign speeches. Despite all this good, *ER* must be financially successful and please its sponsors. So is there a conflict of interest?

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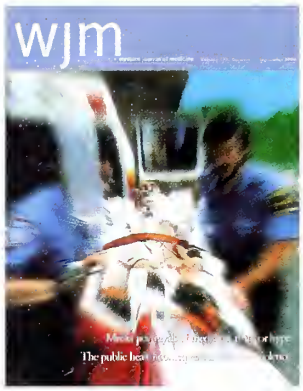

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Op-Ed

Should physicians give tPA to patients with acute ischemic stroke?

For: Thrombolytics in stroke: whose risk is it anyway? see also p 149

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Stroke remains the leading cause of long-term disability in the United States. One third of stroke patients presenting with severe disabilities cannot care for themselves. By 7 years, nearly three quarters of these are unable to return to the work they did before their stroke. Physicians recognize the risks of administering tissue plasminogen activator (tPA) for stroke. Patients, when offered the opportunity to improve their chance of complete functional recovery, are willing to consider the benefits of tPA if it will save them from permanent disability. Difficulties in offering thrombolytics in emergency departments (EDs) are usually reduced to 3 areas of concern: whether the use of tPA actually benefits stroke patients, patients' eligibility to receive it, and whether the development of a "stroke team" in the ED is economically feasible.

In a 1995 National Institute of Neurological Disorders and Stroke (NINDS) trial, patients given tPA had a significant reduction in disability at 30 days, with no difference in mortality. By 30 days, 43% of those enrolled were functionally independent.[1] At 3 months, 50% of those treated had minimal or no disability versus 38% of controls. At 3 months, significantly more patients given tPA had minimal or no disability than those given placebo. By 90 days, 11% to 13% more of those treated with tPA had significant improvements in functionality and reduced disability. One of every 11 stroke patients treated in an ED with tPA will leave the hospital with little or no disability. These results were recently substantiated by a larger trial (Standard Treatment with Alteplase to Reverse Stroke [STARS] Study) involving 57 hospitals.[2] Thrombolytic therapy for acute ischemic stroke is endorsed by the American Academy of Neurologists and the American Heart Association. In severe stroke (NINDS scores >20), the chance of an elderly person having complete recovery increases from 0% to 7% to 8% with tPA. This offsets the 3% increased risk of death, and the increased risk of symptomatic intracranial hemorrhage, associated with the drug.[1]

Like protocols for myocardial infarction, stroke protocols need to be established before thrombolytics can be administered in the ED. Today's emergency physicians are comfortable initiating thrombolytic therapy for myocardial infarction without a cardiologist's approval, but this "comfort in therapy" was born of years of coordinated efforts between the ED and other services. Similarly, a coordinated multidisciplinary effort between emergency medicine, neurology, radiology, and others—to form a stroke team—may be needed. With stroke, strict adherence to inclusion and exclusion criteria for giving tPA has reduced complication rates.[2,3] In the STARS trial, the rate of symptomatic intracranial hemorrhage from tPA was only 3.3% in those properly enrolled. In comparison, the rates of symptomatic intracranial hemorrhage occurring with tPA treatment in patients with myocardial infarction are about 1%. Coordinated stroke protocols can reduce such hemorrhage rates, while also reducing treatment times and protocol violations.[2,3]

The argument that developing a stroke team would benefit only a few patients while draining substantial hospital resources is also shortsighted. Thrombolytic agents are now used in 17% of patients presenting with acute ischemic stroke at the Hermann Hospital, Houston, Texas, and are 3 times more likely to be indicated for acute stroke than for myocardial infarction at our institution. Satellite hospitals in our area, without 24-hour ancillary services, give thrombolytic therapy for 3% to 7% of patients presenting with stroke and then transfer those patients to larger centers for continuing stroke care. Although we use tPA more commonly than elsewhere in the United States, early recognition of stroke and increased public awareness will likely increase eligibility rates, as it did in our area. Ignoring the benefits of aggressive stroke management, with the assumption that a therapeutic plan or team cannot be conveniently assembled during the therapeutic window, may no longer be a valid response in an informed community. The actual start-up cost of establishing an acute stroke team is remarkably low—$5,000 to $10,000[4]—and this can be recovered within a year of its operation.[5]

Early focused neurologic care is clearly beneficial with or without thrombolytics. A meta-analysis of organized stroke teams demonstrated a 5.6% absolute reduction in the incidences of death and dependency.[6] This suggests that establishing a stroke team is cost-effective. Reduced lengths of stay and rehabilitation savings offset the start-up costs of an in-house stroke team. The drug may lead to cost savings of $600,000 per 1,000 patients treated.[5]

Delivering quality medical care requires knowledge of the risks of a procedure and identifying those who may benefit from a medical or therapeutic modality. An approach that significantly reduces long-term disability in 564 of 1,000 patients over a span of 30 years, while demonstrating long-term economic benefits in more than 90%, must be considered a therapeutic option.[5] Physicians are well versed in a patient's right to refuse an inter-

vention. However, physicians acting in patients' best interests must also acknowledge the patients' right to consider a treatment with long-term benefits. If physicians withhold tPA from eligible stroke patients, they are denying them a treatment that reduces the risk of long-term disability. The devastating outcomes after stroke should always be weighed against the potential benefits of giving tPA.

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Should physicians give tPA to patients with acute ischemic stroke?

Against: And just what is the emperor of stroke wearing?

see also p 148

An intervention is *efficacious* if it produces more benefit than harm in the idealized setting of an expert-based study. It is *effective* if it is beneficial in daily clinical practice. Despite the enormous propaganda machine pushing the exciting new fashion of thrombolytic therapy for acute ischemic stroke, there is good reason to question the efficacy of such therapy and overwhelming reason to question its effectiveness.

With regard to efficacy, of 7 randomized controlled trials (RCTs) of thrombolysis to date,[1-7] only 1—the NINDS study—showed benefit in any primary clinical outcome measure.[1] The NINDS study, which made use of specialized expertise, included just over 300 patients who received tPA. The absolute benefit in the 3-month outcome (12%-13%) was modest, especially since 95% or more of stroke patients seen at study centers were not even eligible for inclusion. There was no mortality benefit from tPA in the trial, nor was there benefit in the other primary outcome of "substantial recovery" in the first 24 hours. On the basis of the NINDS study, thrombolysis could only help, at most, 1 of every 125 stroke patients.[8] Given that NINDS artificially inflated the number of patients seen early after the onset of symptoms—those seen in less than 90 minutes—even these estimates are conservative.

But there are many reasons to be skeptical about the NINDS trial, even though it is methodologically sound. Among innumerable examples of drugs for which a single trial suggests benefit, but subsequent and more substantial work ultimately proves that this is not the case, perhaps the most relevant to this discussion is the use of low-molecular-weight heparin for acute ischemic stroke. A study by Kay and colleagues, published as the next article in the very same issue of the *New England Journal of Medicine*,[9] had both a similar number of patients and a similar effect size as the NINDS trial. It did not receive a fraction of the publicity that the NINDS trial did, and alas, when the use of low-molecular-weight heparin was studied further in a far larger RCT, it proved to be without benefit. No similar follow-up RCT, to validate or challenge the NINDS trial findings, has been done, nor is one likely.

Furthermore, other RCTs of thrombolytic therapy in acute ischemic stroke have been done, the results of all of which have been either neutral or negative, and several found statistically and clinically important increases in mortality. This may be because the risk-benefit equation for thrombolysis is favorable only under the specific conditions (timing, dose, etc) of the NINDS trial. Without a single confirmatory RCT, however, an equally plausible explanation is that the disparity in results is due to chance. When similar trials are repeated many times, results will occasionally appear particularly good, particularly bad, or everywhere in between.

An even greater concern is that the effectiveness of thrombolysis in general community practice will be far less than any efficacy it achieved under the idealized circum-

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stances of the NINDS trial. Given the relatively small benefits found in the NINDS trial, even a small diminution of benefit, or increase in harm, could translate into overall harm to patients.

Patients misdiagnosed as having a stroke, who actually have a "stroke mimic"—such as Todd's paralysis, infection, or metabolic disorder—(none of which are identified by CT) can only be harmed by thrombolysis. Although stroke mimics were rare in the expert-based NINDS trial, they are far more common in community practice.[10] Thrombolysis will surely harm patients with an unrecognized hemorrhagic stroke, and few emergency physicians, neurologists, or general radiologists are able to identify all or even most subtle hemorrhages.[11] The use of thrombolysis more than 3 hours from the onset of symptoms is associated with worse outcomes and would also skew the risk-benefit ratio. Given the lesser resources in community practice and the pressure to treat patients at least occasionally, many patients with unrecognized hemorrhage are bound to be included, with predictable consequences.

Several groups that participated in various RCTs of tPA have published glowing reports about continued "success" outside an ongoing trial, which they note is statistically "consistent with" the NINDS results. Their claim that this is testimony to the effectiveness of thrombolysis is not appropriate, however, for many reasons. Such groups are not representative of standard community practice. Their results may reflect publication bias—only the groups with good results publish them. Their numbers are so small that virtually any outcomes are "consistent with" the results from the NINDS trial, as well as with terrible outcomes. Their outcomes are not measured by blinded observers and thus may reflect the enthusiasm, and bias, of the authors.

The only realistic effectiveness study published to date paints a very different picture of the effect of thrombolysis in community practice.[12] This trial included results from every stroke patient treated with tPA in essentially all the hospitals in Cleveland, Ohio, and thus was neither selective in its reporting nor reliant only on expert practitioners. It found, predictably, that many patients were treated inappropriately, that the rates of symptomatic and fatal intracranial hemorrhage were astronomic, and that the outcomes—including mortality—were far worse than would be predicted had these patients received only conservative therapy.

It would not be unreasonable to encourage widespread use of a new therapy, even in the absence of clear-cut evidence of benefit, for a condition in which the following conditions exist:

- outcome is virtually uniformly bad with standard therapy,
- the potential benefits of the new therapy are substantial,
- the proposed treatment is unlikely to cause harm, and
- there is no reason to suspect results will be substantially worse in general practice than they are in expert-based studies.

For thrombolysis in acute stroke, none of these conditions apply.

Although it is possible that individual patients with acute ischemic stroke may indeed benefit from thrombolysis, and such "saves" would be cause for celebration, creating fatal or devastating hemorrhage in other patients is equally tragic. Until there is better reason to think that the widespread use of thrombolytics would do more of the former than the latter, we should all ask why there's such a big parade and so many admirers of tPA's newest fancy clothes.

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Reproductive health care is marginalized

Primary care physicians are in a unique position to lobby for services

Soon after I arrived in Washington, DC, people asked me—a British woman—what the law in my country was on abortion. I explained that if you wanted to terminate a pregnancy, you went to your primary care physician or to the local family planning clinic, where everything would be arranged. The National Health Service pays for this procedure. There are no placard-carrying antiabortionists outside the clinics getting in your way. Abortion is not a major issue in Britain—it is just a necessary, albeit unfortunate, part of life. I never thought that it had anything to do with politics.

In the United States, I was shocked to find that all aspects of reproductive health are seen as political—even sex education and contraception. In 1997, Congress, which was cutting public spending, voted to spend $250 million on abstinence-only sex education. Everyone in the country has an opinion on abortion.

The result of the personal being made political is that, despite US law supporting a woman's right to make reproductive choices, a woman who chooses to terminate a pregnancy may find it extremely difficult to do so. In 86% of US counties, there is no physician to provide abortions.[1] Only 14% of US hospitals permit abortions to be performed at the faciliry, and many of these are done only in very limited circumstances.[1] One in 10 women has to travel more than 100 miles to find an abortion provider.[2] In 31 states, young women must have parental permission or notify their parents before having an abortion, and 14 states have statutory waiting periods.[3] Medicare and Medicaid do not cover abortions, except in cases of rape, incest, or if the life of the woman is in danger. Military women serving overseas cannot have an abortion in an American hospital, even if they pay for it themselves.[4] The list of barriers to women wanting basic health care continues to grow.

As the political and legal debate continues, the lives of real women are affected. During the 4 years I worked for Choice USA, a prochoice education and activist organization, I met many such women. Their histories are now in the public domain. There are the 15-year-old best friends who were gang raped, and both became pregnant. One was able to talk to her parents—a legal requirement before an abortion can be obtained—and the termination went ahead. Her friend shot herself dead because she was too scared to tell her parents about the pregnancy. Then there is the woman in Texas on the heart transplant list who was refused an abortion in her hospital. The hospital offers a termination only if the risk of dying due to continuing a pregnancy is higher than 50%. Her risk was just under 50%. I also remember a young woman who ended up having an abortion well into the second trimester because it took her months to negotiate all the barriers that were placed in her way.

What can be done to reverse this marginalization of women's reproductive health rights? Medical professionals are in a unique position to contribute in ways that others cannot.

First, they can publicly support colleagues who provide abortions. There are so few abortion providers partly because elements in the antichoice movement have harassed, bullied, injured, and killed health professionals because of the job they do. Abortion services have consequently been sidelined, making them even easier targets. Medical professionals can address this by publicly supporting abortion providers and advocating for the provision of abortion in hospitals. If every primary care physician had information on the whole range of pregnancy options (including abortion), if every hospital provided abortions, and if every medical student was taught how to perform an abortion, then the target would be too big for the antichoice movement to attack. Antichoice activists and terrorists cannot bomb every hospital, cannot blockade every clinic, and cannot harass every physician and medical student.

Second, medical students, trainee midwives, and clinicians can choose to learn how to perform an abortion if it is offered as part of their training. If they are not offered this, they can campaign to have abortion training pro-

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vided. At present, only 12% of obstetrics-gynecology programs require abortion to be learned, 56% have it as an option, and 26% do not even have it as an option.[5] When abortion is twice as common an operation as tonsillectomy in the United States, it is frightening to think that physicians are not trained how to perform them.[6,7]

Third, primary care physicians can display literature in their clinics highlighting the whole range of reproductive health care options—including abortion and adoption. They can build links with local family planning organizations and abortion providers and can make condoms freely available to their patients.

Fourth, physicians can support prochoice students. Medical professionals are ideally qualified to give advice to pregnant students who want to know their options and to participate in education and training activities.

Finally, they can vote prochoice. The general election in November is of particular importance because it is likely that the next president will appoint several new Supreme Court justices. There are currently 5 prochoice and 4 antichoice justices. The reproductive choices of American women will be severely limited if an antichoice president appoints antichoice judges to the Supreme Court.

I returned to Britain more aware of the problems with the British legal position on abortion and of the geographic variations in service provision—it is far from perfect in the United Kingdom—but even more thankful that the British public support women having choices. I am continually heartened that the debate has remained out of the political arena. We have had only 1 vote in our parliament on abortion since 1967, when abortion was made legal, compared with the 239 votes in Congress since *Roe v Wade* in 1973.[8]

What scares me coming back to the UK is the evangelic antichoice US organizations that have begun to spring up in Britain and the tactics of violence and intimidation that they are using to try to close our clinics and scare our professionals. There will be a massive grassroots response to their tactics of hate. This response will ensure that unnecessary and complicated barriers are not erected to prevent pregnant women having access to all the options and all the medical services they need. Abortion is a mainstream medical service. We will not let Britain go the way of the United States and have reproductive health care marginalized.

Medical professionals who wish to become involved in the prochoice movement can contact the National Abortion Federation ([202] 667-5881). Medical students can contact Medical Students For Choice ([510] 540-1195).

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Medicine in the 1800s

The truth is that medicine, professedly founded on observation, is as sensitive to outside influences, political, religious, philosophical, imaginative, as is the barometer to the changes of atmospheric density. Theoretically it ought to go on its own straightforward inductive path, without regard to changes of government or to fluctuations of public opinion. [But, there is] a closer relation between the Medical Sciences and the conditions of Society and the general thought of the time, than would at first be suspected.

Oliver Wendall Holmes
Currents and Counter-currents in Medical Science, 1860

How can a man spend his whole life in seeing suffering bravely borne and yet remain a hard or a vicious man? It is a noble, generous, kindly profession, and you youngsters have got to see that it remains so.

Arthur Conan Doyle
The Surgeon Talks, 1894

In the Public Eye

News and Features

US cancer institute funds trial of complementary therapy

Deborah Josefson, San Francisco

The US National Cancer Institute, through its office of Complementary and Alternative Medicine, is funding phase III clinical trials of a controversial treatment for advanced pancreatic cancer.

The treatment protocol, the Gonzalez regimen, involves a program of dietary modification, nutritional supplements, and "detoxification" through coffee enemas. Patients with stage II-IV pancreatic cancer are being enrolled.

The study was established in 1993, when Nicholas Gonzalez submitted selected unpublished results of his cancer therapy to the National Cancer Institute. The initial cohort treated with his regimen comprised 11 patients with diverse cancers.

Anecdotal evidence led Gonzalez to concentrate his efforts on pancreatic cancer, which he thought was more responsive to nutritional therapy than other types of cancer.

Preliminary data showed that patients with pancreatic cancer who were treated by the Gonzalez regimen survived an average of 17.5 months longer than those receiving conventional chemotherapy.

On the basis of the results of this preliminary study, 90 patients with pancreatic cancer refractory to surgery were randomized to 1 of 2 arms: 45 patients received intravenous chemotherapy with gemcitabine hydrochloride, a nucleoside inhibitor, for 30 minutes once a week for 7 weeks; the other 45 patients ingested up to 150 dietary supplements daily and took coffee enemas. The supplements included animal glandular extracts, vitamins, trace minerals, papaya, and magnesium citrate. Pancreatic enzymes were also administered.

Both the study and its sponsors are controversial. Detractors point out that, although Gonzalez is a physician, he has never gone beyond the medical degree in terms of residencies or board certification.

His protocol, moreover, is based on a theory promulgated by the Scottish anatomist John Beard in the early years of the last century and popularized by a dentist, William Kelley, in the 1980s. This theory holds that cancer is one disease emanating from ectopic germ cells, which are allowed to grow as a result of a deficiency of proteases.

According to this theory, supplemental treatment with pancreatic enzymes is required to digest the cancerous cells. Coffee enemas are given to "stimulate" the liver to detoxify the cancers and to reduce the incidence of the tumor lysis syndrome.

This theory flies in the face of the modern understanding of neoplasia, which sees cancer as multiple diseases with genetic and environmental bases.

Despite unproved theories, the alternative regimen has received attention and an aura of credibility. Pancreatic cancer is rarely curable, so any regimen that has shown a possibility of increasing survival is worth studying.

Moreover, the National Center for

Dietary supplements, including papaya, are part of the protocol in treating pancreatic cancer

Complementary and Alternative Medicine is mandated to fund alternative and complementary treatments and subject them to the same rigorous review as conventional treatments. The phase III trial is being conducted through a $1.4 million grant given to Columbia University's Rosenthal Center for Alternative Medicine in New York. It is expected to run for 5 years.

Mouth-to-mouth ventilation does not improve CPR

Scott Gottlieb, New York

When performed by a bystander, cardiopulmonary resuscitation (CPR) with chest compression alone provides similar survival to standard CPR with chest compression plus mouth-to-mouth ventilation in sudden cardiac arrest, according to a new study.

Researchers at the University of Washington in Seattle compared the outcome of 520 cases of cardiac arrest outside the hospital. In each case, a bystander was randomized to receive telephone instructions from a fire department dispatcher that were standard CPR instructions with mouth-to-mouth ventilation or instructions for chest compression alone. Instructions for compression took only 1.4 minutes less than instructions for compression plus mouth-to-mouth breathing, the report indicates.

Overall, 64 patients, 29 (10.4%) in the mouth-to-mouth breathing group and 35 (14.6%) in the chest compression-only group survived to the point of discharge from the hospital, the authors report. This difference was not significant, and adjustment of the results for the patient's age, race, location, fire department response time, and other factors in a logistic regression model yielded similar results (*N Engl J Med* 2000;342:1546-1553).

"This challenges preconceived notions, but provides some proof that the challenge is realistic. I think people need to think rationally and carefully about the process of teaching and performing the various components of CPR," said lead author Alfred Hallstrom, director of the Clinical Trials Coordinating Center in Seattle, which is affiliated with the University of Washington.

Enrollment in the study, which ran from January 1992 to August 1998, totalled 1296 cases of cardiac arrest. However, 776 cases were excluded for various reasons, the most common being misdiagnosis of cardiac arrest and arrest due to drug overdose or alcohol intoxication.

In an editorial accompanying the study, Gordon A Ewy of the University of Arizona Sarver Heart Center called the paper a "landmark study" that "will encourage efforts to re-evaluate the way we teach and perform basic CPR." He said that simplification of CPR instructions would be beneficial: "Authorities in CPR have come to realize that our standard method of performing basic CPR is difficult for the average layperson to learn, retain, and perform" (*N Engl J Med* 2000;342:1599-1600).

Mouth-to-mouth resuscitation should not be abandoned, however, according to a statement from the American Heart Association. "A trained rescuer is very likely going to increase the chances of survival by doing mouth-to-mouth along with chest compression," said Jerry Potts, director of science for the Association's Emergency Cardiovascular Care Program. "People should be taught both components of CPR and be able to respond quickly if someone near them has cardiac arrest."

James Hermit, Glasgow

Resuscitation methods being demonstrated

France heads WHO's health systems league table

Zosia Kmietowicz, London

If you are going to be ill, the best place to be is France—the country ranked first in an analysis of the world's health care systems carried out by the World Health Organization (WHO).

Among major countries, France was followed by Italy, Spain, Oman, Austria, and Japan, with several small countries (including San Marino, Andorra, Malta, and Singapore) rated among the top 10 health care providers.

The analysis, which used 5 performance indicators to measure health systems, showed that it is not what you spend on health care but how you spend the resources available to you that is important.

Despite spending more of its gross domestic product on health than any other country, the United States ranked only 37 out of 191

WHO member states; the United Kingdom, which spends just 6% of gross domestic product on health services, was 18th.

The surprise finding of the analysis, said Christopher Murray, director of the WHO's global program on evidence for health policy, was the vast underuse of resources available and the tremendous range of health systems. "Some countries are only performing 20% of what they could achieve while others are 99% efficient," he said.

Oman, which has reduced its child mortality from 230 per 1,000 to 15 per 1,000 in the past 20 years, and Colombia, which was judged the fairest financing system, have seen dramatic improvements in their health care systems as a result of focused investment.

Most of the countries that placed lower—in sub-Sahara Africa—performed badly because of the havoc wreaked by HIV and AIDS, which have reduced life expectancy to less than 40 years in many countries.

One of the key recommendations of the report is to fund health service through prepayment schemes, such as taxes, insurance, or social security, rather than out-of-pocket expenses when people receive their health care.

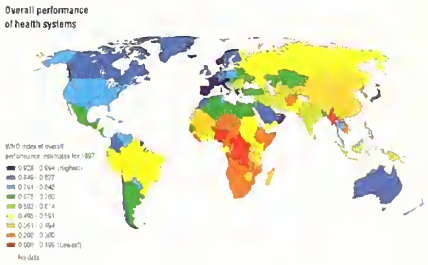
"In many countries without a health insurance safety net, many families have to pay more than 100% of their income for health care when hit with sudden emergencies. In other words, illness forces them into debt," said Julio Frenk, executive director for evidence and information for policy at the WHO.

The report attributes the failings of many health systems to a variety of factors, including "black markets" and "moonlighting," the practice of doctors working simultaneously for the public and private sectors.

"We are trying to help countries improve their performance and we have devised a method that makes it possible to see how well resources are being used rather than the dismal conclusion that poor countries are doing worse than rich countries," said Murray.

"Our real objective is to find out the best way of managing a health service based on sound scientific evidence. For example, we want to build up objective measurements so that we will be able to see whether the purchaser-provider split, as introduced into the United Kingdom, really helps to achieve better health."

The analysis, which took 2 years to complete, will be an annual event.



World Health Organization

Figure 1 The United States leads in spending but trails in performance for health care

The World Health Report 2000—Health Systems: Improving Performance is published by the WHO and can also be accessed at www.who.int/

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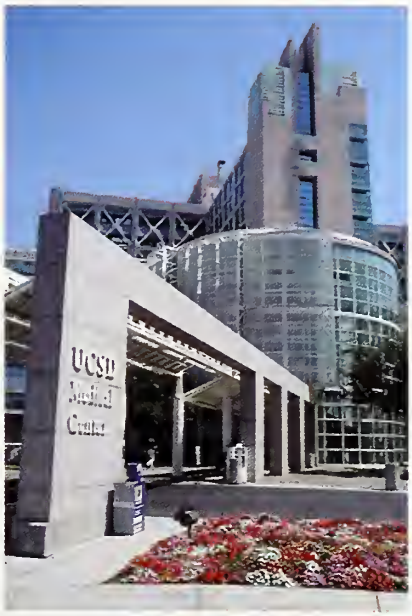

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Media Watch

Challenging *ER*'s psychokiller

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Competing interests: None declared

Slightly modified from an article published in *BMJ* 2000;320:1282

ER, the US television drama of high-adrenaline medical heroics, has blazed its way into a 6th season. It has undoubtedly captured the public imagination, with its strong characters, uneasy tensions, and frenetic trauma calls. Highly positive images of health care professionals are presented to a huge number of viewers. This year, in the week starting January 18, it was seen in 21 million of a possible 99.4 million US households.

Two infamous episodes involving the double stabbing of medical student Lucy and resident Carter caused public excitement, sadness, and even grief. In the first, we saw Lucy working up the case of a young married man, Paul, who had presented with headaches. Carter offers minimal supervision. When the man becomes disoriented, Lucy carries out a lumbar puncture while Carter holds him down. All examination and test results are normal, and when Paul's college friends describe a recent increase in bizarre and suspicious behavior, a psychiatry consultation is requested. The psychiatrist is busy, so Paul remains untreated in a secluded side room. The episode ends with Paul's unprovoked and vicious assault on the medics. Carter falls to the floor to see Lucy bleeding to near death under the patient's gurney.

In the second episode, we saw the brutal resuscitation and harrowing surgery of both victims. In the midst of this clinical chaos, Paul returns. He had escaped the hospital but was hit by a car. Although Paul is clearly psychotic and has life-threatening injuries, consultant Dr Weaver cannot bring herself to treat him and hands his care over to a colleague. Lucy awakes postoperatively, and true to form, she diagnoses a pulmonary embolus in herself and then dies. Carter survives.

This was undoubtedly a dramatic and powerful storyline. But after seeing the episodes, we became concerned about *ER*'s portrayal of mentally ill people. Did it only ever show them as violent and dangerous? We went back and watched 22 consecutive episodes to see how psychiatric patients were represented.

MENTAL ILLNESS AS PORTRAYED ON *ER*

In these episodes, 28 patients are portrayed with psychiatric problems, most often substance misuse. Six are psychotic. One man smashes his car with a baseball bat because "demons" are telling him to harm his wife. A woman who thinks she is a bird is brought into the emergency department in a huge birdcage. The administration of haloperidol is advised before bolt cutters are obtained to release her. A woman masquerading as a physician stalks a male staff member as part of a delusion of erotomania.

Five patients deliberately harm themselves, mostly through destructive acts such as cutting. One man encourages another to drill a hole in his forehead, and a depressed woman threatens to harm others. A man with mental health problems shoots his wife and children, and a patient with similar problems kills a police officer.

Four children are shown with attention hyperactivity disorder and 4 adults with post-traumatic stress disorder, 1 of whom becomes aggressive when recollecting the traumatic experiences. One child kills another, and there is a suggestion that he has psychological problems because a psychiatry consultation is requested. The 1 suicide is an extreme situation in which a man first rapes a comatose patient and then hangs himself.

Channel 4

THE MESSAGE TO VIEWERS

These examples suggest to the audience that mentally ill people are nearly always destructive, either to themselves or others. The dominant theme is of threat. Although emergency psychiatrists do see violent patients, *ER* clearly overrepresents this danger. More important, it fails to offer an empathic view of the distress that mental illness causes to sufferers. We fear that many viewers will share Dr Weaver's revulsion at the "psycho" who killed Lucy and maimed Carter. Even depressed and suicidal patients are shown harming others.

The series, in making such a strong association between psychiatric illness and violence, is following established trends in television news, drama, and the tabloid press. It is adding to the process of stigmatization by the media.

The US National Alliance for the Mentally Ill (NAMI), a self-help and family advocacy organization, campaigns against this media stigmatization. Stella March, of the NAMI "Stigmabusters" campaign, said of the *ER* stabbing episode, "We found this episode to be deeply troubling for the association it made between mental illness and violence, as did many, many NAMI members who contacted us after the show."

ER features strong stories with harrowing images. These fail to offer a sympathetic view of people with mental health problems. It is too late to object formally to the producers, and we are not suggesting censorship. The irony here is thar this series achieves a high degree of realism when it deals with medical and surgical emergencies. Would that it would offer the same degree of accuracy in its portrayal of psychiatry. Where are the cases in which patients are helpfully supported through the terror and distress of their acute illness?

The series, in making such a strong association between psychiatric illness and violence, is following established trends in television news, drama, and the tabloid press

The proportion of homicides committed by mentally ill people in Britain has fallen annually since 1957. The challenge now is to propagate some positive media stories, creating more accurate images to capture the public imagination.

COMMENTARY
Clanging critics

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West J Med 2000;173:157-158

Television depictions of individuals with psychiatric disorders have recently received increased media attention, particularly after the premiere of the ABC series *Wonderland,* which showed the day-to-day workings of a psychiatric hospital in New York City. That series was cancelled after only 2 airings owing to poor ratings. Even so, those 2 episodes generated vehement criticism from the National Alliance for the Mentally Ill (NAMI) and others for depicting psychiatric patients as violent and frightening, although television critics in general lauded the series. Condren and Byrne, in their critique of *ER,* raise similar points about the portrayal of psychiatric patients as "violent and dangerous" and "nearly always destructive, either to themselves or others."

We take issue with many of the authors' overgeneralizations and frank misstatements about the presentation of psychiatric patients on *ER.* We have always sought to portray a variety of patients on the show, and as such, some psychiatric patients are violent, but most are not. By focusing on 1 patient, a man with schizophrenia who killed the character Lucy Knight and injured John Carter, the authors jump to the false conclusion that we are somehow saying that all people with schizophrenia are violent and dangerous.

Violent patients in the emergency department are likely to be under the influence of alcohol or drugs, psychotic, or suffer from a personality disorder, mental retardation, or an organic condition.[1] Although "violent behavior in psychiatric patients is no higher than in normal patients . . . paranoid patients are especially worrisome, particularly when they shift from generalized paranoia . . . to a specific person or group."[2] Paul Sobriki, the character with schizophrenia portrayed on *ER,* presented with headaches that were misdiagnosed as meningitis. As Lucy and Carter attempted a lumbar puncture, Paul begged them to stop, pleading: "What're you putting into me? Stop, it hurts . . . You're sticking me in my back . . . You're sticking me. Stop hurting me!" Carter and Lucy should have recognized that their kicking and screaming patient was not a typical presentation for an adult undergoing a lumbar puncture. That was a terrible mistake on their part and on the part of the attendings, which was dealt with in the following episode. However, we were careful in setting up Paul's paranoia so that when a knife was available (it was lying beside a Valentine's cake), Paul picked it up and

used it against the 2 characters he perceived to be his tormentors. To say, then, that the episode ends with Paul's "unprovoked" assault fails to take into account the careful depiction of his psychosis. Were we saying that everyone with schizophrenia stabs their physician? Hardly. We were showing 1 case, and only 1 case.

What is particularly misleading about the authors' critique is that they use the episode in which Lucy and Carter are stabbed as a straw man for performing what turns out to be a selective and highly misleading retrospective analysis of previous episodes dealing with psychiatric issues. Their subtextual premise is that if 1 episode showed a psychotic patient being violent, then all others must do the same.

We find it strange, yet convenient for their premise, that the authors failed to mention several episodes within the previous 22 that depicted a woman with schizophrenia, Coco, who gave birth to a baby and was helped by Nurse Hathaway not only to stay on her medications but to learn how to care for the infant. Coco was psychotic when she delivered the baby on the street, but in 2 later episodes, Hathaway worked with her so that she could keep her baby. The message: a woman with schizophrenia can be treated successfully with medication and, in this case, can be trusted to care well for her baby with some supervision.

Rather than address each example the authors give to bolster their spurious argument that *ER* depicts "mentally ill people [as] nearly always destructive, either to themselves or others," we will highlight the most egregious. First, one of the "hyperactive" children, Seth, a boy of 11 who cut himself when he angrily smashed a window, was found by Lucy not only to be depressed but taking a combination of drugs (Mellaril [thioridazine hydrochloride], Inderal [propranolol hydrochloride], and clonidine hydrochloride) that was causing severe side effects. Lucy learned this by taking a thorough history and by listening empathetically to Seth. She even asked the psychiatric attending if she could follow up with Seth on a regular basis to be sure he was doing all right. "Where are the cases in which patients are helpfully supported through the terror and distress of their acute illness?" the authors ask. These are 2 of many examples. Why did the authors, once again, fail to note this? Because it clashed with their half-baked theory that *ER* for some reason only presents psychiatric patients as inhuman monsters.

Some of the examples cited are not to be taken as seriously as the cases of schizophrenia or depression. The episode in which "one man encourages another to drill a hole in his forehead" was played as bizarrely comical, as was the one of the woman who thought she was a bird. The show does take place in an ER after all, where all modes of human behavior are seen.

On *ER* we strive to show an array of medical and psychiatric problems that pose interesting treatment and ethical dilemmas to the doctors and nurses. We consult regularly with psychiatrists from the National Institutes of Health, UCLA, and Harvard to ensure that our depictions are realistic and responsible. We have recently shown how difficult it is to treat anorexia and bulimia and, in the past, have presented patients with depression, bipolar disorder, and drug addiction. In fact, a major story line now for *ER* is depicting John Carter's drug addiction and treatment. Last season, the doctors failed to notice his problem until a medical student caught Carter injecting himself with fentanyl. Then, all the doctors worked together to intervene and to save Carter's life and career. Need we say more about compassion and empathy?

In the future, we hope that researchers take a less selective view of the show to bolster their simplistic claims. We welcome debate and responsible dialogue about the depiction of psychiatric patients, and we certainly will strive in the future to be more compassionate in our portrayals, particularly because viewers do form opinions about psychiatric illnesses, at least in part, by what they see on television. We ask in return that researchers like Condren and Byrne present a fairer analysis of the stories. After all, we share the same goal: to portray psychiatric disorders honestly, informatively, and with empathy.

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On earth as it is in hell

Hollywood's view of paramedics at work

Two recent movies, *Broken Vessels* (A-Pix Entertainment) and *Bringing Out the Dead* (Touchstone), portray the lives of those who work for the emergency medical services in urban America. Or at least they claim to.

Broken Vessels tells the story of Tom (Jason London), an emergency medical technician who arrives in Los Angeles while trying to escape his past in Altoona, Pennsylvania. He lands a job as an ambulance driver and is teamed up with Jimmy (Todd Field), a senior Los Angeles paramedic whose best skill seems to be snatching his sunglasses off his face and trying to look cool.

Within 10 minutes of the start of the movie, the 2 paramedics are drinking alcohol, picking up women, having sex, buying heroin on the street corner, and getting high—all while on duty, mostly in the ambulance. They then start stealing from their patients to support their drug habits and eventually run afoul of a drug dealer, who in turn tries to shoot them. As they speed away in the ambulance, they crash quite spectacularly. Jimmy is killed, and Tom decides he has to become more responsible.

Bringing Out the Dead tells the story of Frank Pierce (Nicolas Cage), a paramedic in New York City who is haunted by the ghost of a young girl named Rose whom he was

Bringing Out the Dead, Paramount Pictures 1999

unable to resuscitate following an acute asthmatic attack. He sees her face on nearly every woman he encounters, and he is certain that all he needs is to save one person's life to move beyond the memory.

When Frank resuscitates the elderly Mr Burke (Cullen O Johnson), he falls for Burke's daughter Mary (Patricia Arquette). Unfortunately, Burke's recovery is minimal; he is kept alive only by life support and becomes an additional burden to Frank. There is hope for absolution when Frank and his partner Marcus (Ving Rhames) deliver twins from a woman, while her boyfriend stands by and swears that they are both virgins. But one of the babies dies, and so Frank's haunting continues. Ultimately, he overcomes the ghosts by disconnecting Mr Burke from his ventilator and allowing him to die peacefully.

Broken Vessels is a movie about partying, drinking, and drug taking, and the main characters just happen to be paramedics. That the movie is set primarily in an ambulance adds nothing to the stoty line, but it does allow amazing cinematography involving flashing red and white lights and blurred images. The film focuses on drug addiction, rather than the life and role of paramedics, so it likely will not have much effect on the public's perception of these professionals.

Martin Scorcese, director of *Bringing Out the Dead,* also uses striking images, casting a glowing aura around Cage's character. In contrast to *Broken Vessels,* however, Frank Pierce's job as a paramedic is central to the film's plot. Indeed, through the first half of the movie, we get to know him as a compassionate and competent provider of emergency medical care.

It is, therefore, more disappointing when he and Marcus have a drink in the ambulance to celebrate the "virgin birth," when he follows Mary to a drug den and indulges in its offerings, and when he and another paramedic go hunting for someone to beat up in order to vent their frustrations. Unfortunately, the audience is likely to accept Cage's portrayal of a paramedic, and to extend their perceptions of his character to the profession as a whole.

Both of these movies have glimmers of reality, mostly in their depiction of the emergency scenes and the interactions between paramedics, law enforcers, firefighters, and bystanders. They also go some way in portraying the frustrations of the work schedule and the divergent segments of society encountered by ambulance crews. Even some of the more despicable traits of the paramedics might not be that far fetched. But the difference between true life and these movies is that in reality—for the most part—no single call, no single shift, no single patient, and no single paramedic manifests all of these characteristics. Not even in Los Angeles or New York City.

These films are almost saved by their moments of humor. But they do not accurately describe the life a paramedic in big-city America. Urban legends—or perhaps urban myths—make for better stories. The real lives of us paramedics can be, in contrast, rather mundane.

Lawrence Brown
Syracuse, New York

capsule

Cartoons contain violence *wjm* editors love feature-length cartoons and we are grateful to *JAMA* (2000;238:2716-20) for printing a comprehensive list of all those released since 1937. A content analysis describes all the films as violent to a greater or lesser extent, and parents wanting to limit their children's exposure should stick to *Winne the Pooh* and *Dumbo,* which contain only 1 minute of violence each. The classic *A Bug's Life* is the second most violent animated film ever released. No doubt grasshoppers account for most of it.

capsule

History repeats itself A historical medical textbook, written by an English monk over 800 years ago, has gone on display at the US National Library of Medicine in Bethesda, MD after an absence of over half a century. The book, which contains many of Hippocrates' famous aphorisms, disappeared under suspicious circumstances sometime in the 1940s. It turned up last year at a rare book market in Southern California. The dealer donated the book to the library after some "decorous wrangling."

Med.Pix

The palms and soles

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None declared

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QUESTION: A 31-year-old homeless man comes to a free clinic, asking if you can get rid of the spots that have appeared all over his body (figure). He tells you that these spots appeared 3 days ago. The spots are not painful and they do not itch. The patient has no other clinical symptoms and feels generally well. With further questioning, he discusses his use of crack cocaine, which has contributed to his homelessness.

A physical examination reveals hyperpigmented macules on the palms, wrists, forearms, soles, and ankles. There is slight scaling on these macules.

What additional questions would you like to ask this patient? What other parts of the body would you like to examine? What tests would help you make the diagnosis? What is your differential diagnosis at this point?

Macules on the hand and foot were not itchy or painful

ANSWER: Taking a sexual history from the patient revealed that he had multiple female sexual partners at the time he was using crack cocaine. Some of the women provided sex for drugs. The genitals and oral mucosa were examined for additional lesions. The patient was found to have mucous patches on the penis and additional macules on the thighs. The patient also had mucous patches in the mouth.

The protean manifestations of secondary syphilis generally start 2 to 8 weeks after a chancre is present. In this case, the patient did not remember having a chancre. In secondary syphilis, 90% of patients have skin manifestations, 35% have oral lesions, 20% have genital lesions, and 70% have constitutional symptoms, including fever and malaise.[1(p2479)]

The lesions of secondary syphilis may be macular, maculopapular, papular, pustular, or annular. They are not vesicular. Macules on the palms and soles are highly suggestive of secondary syphilis. The rash is generally not itchy. About 20% of patients have mucous patches or condylomata lata. Lata, or flat, patches occur on the genitals and are flatter than condylomata acuminata. Some patients have moth-eaten alopecia.

DIAGNOSIS

The differential diagnosis included secondary syphilis, pityriasis rosea (a benign condition that resolves over 6 to 8 weeks), and a viral exanthem. Secondary syphilis was by far the most likely diagnosis.

A VDRL test was performed. In secondary syphilis, the non-treponemal tests VDRL and rapid plasmin reagin (RPR) have a sensitivity of 99%. A confirmatory treponemal test, such as the fluorescent treponemal antibody absorption (FTA-ABS) test, is needed to confirm a positive VDRL or RPR. As recommended by the Centers for Disease Control and Prevention, the patient was tested for HIV with his consent.[2]

TREATMENT

Treatment was recommended that day, even before the result of the VDRL, because of the high likelihood of secondary syphilis. The patient received an injection of 2.4 million units of penicillin G in the buttocks, the recommended dose for an adequate cure of primary and secondary syphilis in immunocompetent patients.[2]

Penicillin is the most effective therapy for all stages of syphilis.[2] Doxycycline hyclate or tetracycline are alternative treatments for patients with a demonstrated allergy to penicillin. Pregnant patients who are allergic to penicillin should be desensitized, if necessary, and treated with penicillin.[2]

The patient, who had no history of penicillin allergy, was observed for 1 hour in the clinic to ensure that he did not have an allergic reaction to the drug. Jarisch-Herxheimer reaction occurs in up to 90% of patients with secondary syphilis who are treated with penicillin.[1(p2488)] The reaction occurs as soon as 1 to 2 hours after treatment as a result of antigen release from *Treponema pallidum* when the spirochetes are killed by the drug. Patients may experience chills, fever, myalgias, headache, tachycardia, hyperventilation, flushing, and mild hypotension for 12 to 24 hours. This reaction is more common in patients with secondary syphilis than in individuals with other forms of the disease, because the secondary form involves the highest number of spirochetes. The reaction is treated with antipyretic medication and rest.

The patient was counseled about safe sexual practices and offered help to stop his crack cocaine use.

OUTCOME

The VDRL test was strongly positive at a titer of 1:512, with a confirmatory positive FTA-ABS test. The patient did not return for a follow-up evaluation, which validated the importance of the decision to administer treatment on the basis of the appearance of the rash. The HIV test was negative. The positive VDRL was reported to the health department for contact tracing and treatment, which proved difficult because the patient was homeless.

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capsule

Face-to-face advice to patients can help Doctors who feel they are wasting their breath giving lifestyle advice to patients should take heart. Research from St Louis suggests that face-to-face advice can prime patients to take notice of health promotion material that would otherwise be ignored or instantly forgotten (*Arch Fam Med* 2000;9:426-433).

Mail

Correcting the record

To the Editor

After the publication of our research paper in 1997,[1] we became aware of a compromise in the quality of part of the data set collected by a study interviewer. A formal review confirmed that the interviewer had created some records that were duplicated or inconsistent. This constituted clear misconduct in 75 of 1,710 interviews. Additional interviews had fragmentary documentation, which could have compromised at least part of 449 interviews.

The original study examined the relationship between subspecialty follow-up for asthma and measures of medical care provision, utilization of health services, and functional status. We analyzed survey responses at a baseline interview and at follow-up interview approximately 18 months later. Subjects themselves reported the specialty of the physician whom they considered the main provider of their asthma care. Adjusting for demographics and asthma severity, allergists were more likely than pulmonologists to provide a peak flow meter for patients or to administer allergy desensitization injections. They were less likely to prescribe high-dose, inhaled corticosteroid therapy or to administer pneumococcal vaccination. After adjusting for the same covariates, no subspecialty association emerged in relation to emergency department visits or hospitalization for asthma. Those who reported that they had switched specialty care providers had statistically worse quality of life and worse physical function as measured by the SF-36.

We have reanalyzed the data, excluding the compromised and potentially compromised records. We determined that 21 of 539 subjects (4%) were out of the original age range for the study. For an additional 135 subjects (25%), re-interview data had major inconsistencies or where telephone billing records did not clearly provide secondary validation of interviews. We, therefore, excluded 156 subjects (29%) in this initial reanalysis.

We then carried out a second, more restricted reanalysis to remove interviews that were too short. We excluded 65 subjects (12%) whose baseline interviews were less than 30 minutes because these interviews could have represented fragmentary records if they were performed rapidly. We used 20 minutes, based on telephone billing records, as a minimum completed time for the follow-up interviews. We excluded 71 subjects (13%) whose follow-up interviews had originally been 15 to 20 minutes.

The final reanalysis was, therefore, limited to 247 subjects. Allergists were still more likely to supply their patients with peak flow rate meters and were less likely to prescribe high-dose, inhaled corticosteroid therapy. After adjusting for covariates, there was still no association between subspecialty type and rate of hospitalization.

In the original study, patients who switched specialists had a worse quality of life, but this difference was not statistically significant in the re-analysis. The association between switching specialist and experiencing worse physical function was statistically stronger in the reanalysis. Detailed statistical information about the reanalysis is available at: http://medicine.ucsf.edu/divisions/oem/asthma_panel/.

Although we found no substantial impact on the principal major findings and interpretation of the previously published paper, I and my coauthors believe that the scientific record should be corrected.

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Reducing errors by increasing legibility

To the Editor

Formal investigation of drug errors began in the United States only after World War II. By the early 1960s, several hospitals had attempted to quantify their drug errors and found that 10% of drug administrations were associated with at least 1 error.

Attempts were made to identify sources of such errors and mechanisms to prevent them. Such mechanisms included better labeling of containers and labeling of individual tablets or capsules, a practice that began in 1963.[1] The Food and Drug Administration made this practice mandatory in 1995.[2]

Nevertheless, drug errors and adverse drug reactions are the fourth leading cause of death in the United States.[3,4] In response to this high mortality and morbidity, the Medication Safety Council of Washington State has urged hospitals to continue their efforts to reduce drug errors. The Council has focused on community-based drug errors and started with those related to physician-pharmacist communications, especially with regard to legibility of written prescriptions.

We believe that additional clinical information added to the prescription itself—known as a notation of purpose (eg, "for cough" or "for headache")—is helpful to pharmacists.

Other states already have such programs in place. Some physicians criticize the initiative, citing concerns about breaching patients' rights to privacy. Nonetheless, Washington State's Medical Association endorsed our proposal and attempted to publicize the initiative.

The Washington State Board of Pharmacy agreed to collect prescription data from before the start of the program and again 2 years after the start. Data were collected for 6,050 prescriptions in 1996, before the program began. Of these, 29% (1,754) already had a notation of purpose, and over half of these were for Schedule II-III drugs.

In 1998, 2 years after the program began, there was no significance increase in the proportion of prescriptions (1,508/5,800, or 26%) carrying notation of purpose. We therefore initiated an educational intervention, but a repeat survey showed no significant increase (1,560/6,000, or 26%) in the number of prescriptions with the additional notations.

Although notations of purpose may be useful in reducing drug errors, there is resistance to adopt this initiative. As an alternative, our legislature passed an anti-scribble bill, which may counter physician resistance.

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Original Research

Violence and its injury consequences in American movies: a public health perspective

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ABSTRACT **Objectives** To evaluate the seriousness and frequency of violence and the degree of associated injury depicted in the 100 top-grossing American films of 1994. **Methods** Each scene in each film was examined for the presentation of violent actions on persons and coded by a systematic context-sensitive analytic scheme. Specific degrees of violence and indices of injury severity were abstracted. Only actually depicted, not implied, actions were coded, although both explicit and implied consequences were examined. **Results** The median number of violent actions per film was 16 (range, 0-110). Intentional violence outnumbered unintentional violence by a factor of 10. Almost 90% of violent actions showed no consequences to the recipient's body, although more than 80% of the violent actions were executed with lethal or moderate force. Fewer than 1% of violent actions were accompanied by injuries that were then medically attended. **Conclusions** Violent force in American films of 1994 was overwhelmingly intentional and in 4 of 5 cases was executed at levels likely to cause significant bodily injury. Not only action films but movies of all genres contained scenes in which the intensity of the action was not matched by correspondingly severe injury consequences. Many American films, regardless of genre, tend to minimize the consequences of violence to human beings.

Violence in popular entertainment media has recently moved onto the public health agenda as the causes, consequences, and prevention of violence have become the subject of urgent social debate. These concerns extend to scenes on television and in the movies in which the injury consequences to the victims of violence appear to be minimal, violence appears to be justified, and violent actions go unpunished.[1] Extensive research and policy discussions about media violence have indicated that, across widely differing forms of programming, television frequently depicts violent actions.[2-4] Yet, whereas research in media violence has a long history, popular American films shown in theaters seldom have been studied empirically.

The American film industry relies heavily on conventional patterns of cinematic treatment called "genres." Leading American films are distributed across 11 distinct genres: action, adventure, animation, comedy, drama, family, horror, romance, science fiction, thriller, and western.[5] In 1994, just 100 of these films accounted for 89% of the domestic box office receipts of $4.5 billion—a figure that does not include revenue from video, cable, and international markets. Violence has long been basic to the definition of the action and western genres, but other genres such as comedy and drama have also increased the amount and severity of violence depicted. Depictions of violence, therefore, are seen by millions of US customers in theatrical release and by additional millions in their international versions, on videotape, and in television reruns.

To offer a perspective on violence in contemporary American movies, we evaluate the occurrence of violent actions and their consequent injuries as they appear in film. The primary goal is to provide an account of the range and intensity of violent actions and the depiction of injuries resulting from these actions.

METHODS

The study sample included all 100 of the top-grossing films released in 1994, identified in *The Hollywood Reporter*'s annual summary of American films.[5] (The year 1994 was chosen for convenience, not because of any prior expectation about levels of violence in that year's films. Titles are listed in this article and in the box.) A computer-driven abstraction instrument was used to control the playing of the laser disk edition of each film and to encode the violence contained within each scene. Coders were 3 advanced graduate students in film and television (B C, K F, T W). After each violent scene, the film was halted and questions regarding that scene were displayed in sequence on the screen. The coding used a hierarchic structure that allowed progressive movement from scenes to actions to injury consequences as a direct function of time. After coders entered their responses, the playing of the film was continued. Data were recorded using an Apple PowerMac 7500, coupled with a Media Max video controller and managed by Filemaker Pro and Paradox. Coders achieved an inter-rater agreement on all variables of 90%.

The scene is the largest unit of dramatic action in a film and defines the context in which violent actions occur in a given time and space. For this study, a violent action in a single scene was defined as the fundamental unit of analysis and included at minimum a single movement made by an initiator of a given action toward 1 or more recipients—for example, a punch thrown or a weapon discharged. Scenes with implicit rather than demonstrable

Film titles included in study sample and not mentioned in text

Abave the Rim
Ace Ventura
Andre
Angels in the Outfield
Baby's Day Out
Bad Girls
Blank Check
Blink
Blawn Away
Blue Chips
Bullets Over Braadway
City Slickers 2
Clear and Present Danger
Carrina, Carrina
Craaklyn
D2 The Mighty Ducks
Disclasure
Drap Zane
Dumb and Dumber
8 Secands
Faur Weddings and a Funeral
Getting Even With Dad
Greedy
Guarding Tess
House Party 3
I Lave Trauble
IQ
In the Army Naw
Intersectian
Interview With a Vampire
Iran Will
It Cauld Happen to Yau
Jasan's Lyric
Juniar
Legends af the Fall
Lightning Jack
Little Big League
Little Giants
Little Wamen
Lave Affair
Majar League 2
Mary Shelley's Frankenstein
Maverick
Milk Maney
Miracle an 34th Street
Mankey Trauble
My Father the Hera
My Girl 2
Naked Gun 33
Nell
Na Escape
Nabady's Faal
On Deadly Graund
Only Yau
Pulp Fictian
Reality Bites
Renaissance Man
Richie Rich
Speechless
Speed
Star Trek Generations
Street Fighter
Sugar Hill
Terminal Velacity
The Air Up There
The Client
The Calar af Night
The Cawbay Way
The Crow
The Flintstanes
The Getaway
The Jungle Boak
The Little Rascals
The Madness af King Gearge
The Mask
The Pagemaster
The Paper
The Prafessianal
The River Wild
The Santa Clause
The Shadaw
The Shawshank Redemptian
The Specialist
The War
Threesame
Wes Craven's New Nightmare
When a Man Laves a Waman
With Hanars
Wolf
Wyatt Earp

violence—threats, conspiratorial behavior, or conniving—were not included. A continuous series of the same explicit violent actions by the same character was treated as 1 if of equal severity and involving no new weapon. A change in severity of violence (such as from mild to lethal) or method (from fists to machete) resulted in coding a new action. The action's initiator, the recipient of violence, and the nature of the intention—to kill, disable, dominate, capture, or defend—were identified. Violence toward property rather than people was not analyzed for this article.

The seriousness of each action was rated as minimal force (such as pushing, slapping, chases not involving weapons, dousing with nonlethal substances), moderate force (hitting with a closed fist or with a weapon but without sufficient force to be life-threatening), or lethal force (deadly or potentially deadly violence, generally though not always accomplished with a weapon). The explicitness of the portrayal was rated as none (only antecedents or aftermaths were shown, it occurred off screen, or there was no wounding or expression of force), minimal (little specific attention was given to the action or the wounding itself), moderate (the act included its culmination on the victim, generally an injury or an apparent halt to that character's activity, but the injury itself was not explicit), or full (the entire arc of violence from beginning to end was the subject of the filmmaker's attention during the scene, with graphic representation of victims' injuries). For each violent action, the presence of consequences in the form of depicted bodily injury, medical attention, or both were evaluated. If bodily injury was depicted, the degree of damage to the body was rated as mild (bruises, lacerations, broken bones), severe (maiming, blinding, disfigurement), or critical (fatal wounds). Bodily consequences could be shown without depiction of the violent act. Medical treatment after the injury was scored as present or absent; any attempt by any other character in the film to attend to the victim was included. Each violent action was evaluated as either intentional on the part of the person or persons who initiated the action or unintentional (as in the case of "acts of nature" or apparent "accidents").

Logistic regression analyses were used to determine patterns of seriousness, explicitness, and intentionality of violent actions and injury severity and consequences from injury. To quantify the deviance of each genre from the overall pattern of violent actions with regard to each characteristic, logistic regression models were run to compare films in each genre with all other genres. For purposes of analysis, the 3 genres of action, comedy, and drama—which comprised 81 films in the sample—were considered as unique groups; films in the remaining genres were aggregated.

RESULTS

A total of 2,184 violent actions against people were identified in the sample (table 1). This corresponds to 1 violent action about every 5 minutes; every film in the study sample except 1 (*Quiz Show*, Hollywood Pictures) contained at least 1 violent action. The largest number of such actions in a single film was 110 (recorded in the action

Table 1 *Number (mean, minimum, and maximum) of violent actions per film, by genre*

Genre	No. of violent actions (range)	Mean/film
Action (n = 14)	658 (13-110)	47.0
Comedy (n = 41)	586 (1-81)	14.3
Drama (n = 26)	437 (0-44)	16.8
Other (n = 19)	503 (1-97)	26.5
Total (n = 100)	**2,184** (0-110)	21.8

film *Timecop*, MCA/Universal Pictures). One of the family films (*Lion King*, Walt Disney Productions) had nearly as many: 97 separate violent actions.

The data show that 963 (44.1%) violent actions used lethal force, 817 (37.4%) used moderate force, and 404 (18.5%) used only minimal force. Lethal force was used most frequently in the action genre, in which 56.8% of all violent actions were rated lethal. Explicitness was rated either none or minimal in 1,932 scenes (88.4%) but moderate in 222 (10.2%) and maximum in 30 (1.4%). Included in this last category were scenes from 7 of the 14 action films.

Violence was 10 times more frequently the result of intentional rather than unintentional acts, with 1,991 intentional and 193 unintentional violent actions identified in the entire sample. Intentional violent actions showed an absence of injury consequences more often than unintentional, with 87.0% of intentional and 75.6% of unintentional actions depicting neither bodily nor medical consequences.

At least 1 action with the highest level of injury severity was identified at least once in 13 of the 14 action films, in 9 of the 41 comedies, in 8 of the 26 dramas, and in 9 of the remaining 19 films. Across all films in the sample, 1,897 (86.9%) violent actions showed no consequent bodily injury or medical attention, whereas only 254 showed bodily injury (11.6%), 16 showed medical attention (0.7%), and 17 showed both bodily injury and medical attention (0.8%) (table 2). The presence of bodily consequences was found most frequently in actions using lethal force (71.8%). Actions not depicting injury consequences were more equally distributed by seriousness, with 39.9% of lethal actions, 39.3% of moderate actions, and 20.8% of minimal actions showing no injury consequences.

In 9 of 10 violent scenes, the injury to the victim was not depicted (table 3). When consequences to bodies were shown, however, 118 (54.1%) were critical (for example, dead or dying persons), 55 (25.2%) were severe (broken bones, severe blood loss), and 45 (20.6%) were mild (bruises, slight lacerations).

Two special types of scenes were identified in the analysis: the first of these included scenes in which violent actions of high lethality and their effects on the body of the recipient were both graphically portrayed. A total of 115 scenes, 5.3% of all scenes in which violence was present, fit this description. Such scenes were found in 13 (92.9%) of the action movies, 9 (22.0%) of the comedies, and 8 (30.8%) of the dramas. In the action genre, 1 of every 12 violent actions was of this type. Illustrations were found in 15 different scenes in *Beverly Hills Cop 3* (Paramount Pictures), in 9 different scenes in *Stargate* (Carolco Pictures), and at least once in 37 other films in the study sample.

The other special type comprised scenes depicting violence that would ordinarily result in massive injuries to the recipient but, in the world of film, did not. Such portrayals were found in 797 scenes, or 36.5% of all scenes in which violence was present. As many as 51 such scenes were found in a single action film (*True Lies*, Lightstorm), on average half of all the violent scenes in action movies. Scenes of this type occurred in 57.5% of the comedy films, with 1 comedy film (*A Low Down Dirty Shame*, Hollywood Pictures) depicting such scenes 31 different times. In dramas, this type of scene occurred in 65.2%, with 1 dramatic film (*Natural Born Killers*, Warner Bros) containing 25 separate instances. All but 3 of the films in the remaining genres also included violence of high lethality but without injury; the average number of such scenes in those films was 9.7 per film.

Logistic regression analyses showed that action films had significantly more serious (odds ratio [OR] = 1.2) and more explicit (OR = 1.5) depictions of violence than other genres and also exhibited a greater degree of intentionality (OR = 2.4) (table 4). In action films, however, neither the

Table 2 *Number (%) of violent actions without consequences, with bodily injury, medical attention, or both, by film genre*

Genre	No consequences	Bodily injury only	Medical attention only	Bodily injury and medical attention	Total no. of violent actions
Action	594 (27.2)	57 (2.6)	4 (0.2)	3 (0.1)	658
Comedy	496 (22.7)	83 (3.8)	6 (0.3)	1 (0)	586
Drama	375 (17.2)	49 (2.2)	4 (0.2)	9 (0.4)	437
Other	432 (19.8)	65 (3.0)	2 (0.1)	4 (0.2)	503
Total	**1,897** (86.6)	**254** (11.6)	**16** (0.7)	**17** (0.8)	**2,184**

resulting injury severities nor the number of consequences resulting from injuries were significantly greater or lesser than those in other genres (OR = 0.84 and 0.82, respectively).

In contrast to action films, comedies had lower levels of seriousness (OR = 0.80), lower levels of explicitness (OR = 0.56), and the lowest degree of intentionality of all genres (OR = 0.40). Comedies had average levels of both injury severity and consequences from injuries. Films in the drama genre had higher levels of explicitness (OR = 1.42) and higher levels of intentionality (OR = 1.63) than films in other genres but lower levels of seriousness (OR = 0.84).

DISCUSSION

Two highly consistent features were found in the depiction of violence in the 100 top-grossing American films in 1994: first, film violence was most often an intentional act of 1 character toward another, and second, consequences of violent events were most often omitted. Although most violent actions depicted moderate or lethal force, more than 6 of every 7 violent actions in the study sample contained no portrayal of consequences of those actions, either in terms of bodily injury or medical attention—an illustration being the gang beating of a ninja character in *Three Ninjas Kick Back*, Ben-Ami/Leeds Productions. In the film world, the human body's durability under violent attack is often greatly exaggerated, the links between injury causes and consequences appearing to have been suspended altogether. On the other hand, numerous scenes depicting violent acts raised the violence to maximum levels for both the initiator of the violence and the recipient—an illustration being the Vietnam war sequence in *Forrest Gump*, Paramount Pictures.

Relative to other films, action films had an increased severity of action, coupled with a reduced severity of injury and a general lack of consequences to recipients of those actions. The depictions of violence in the action genre tended to contain a discord between the often extreme severity of the action, coupled with a lack of severity in its consequences. In contrast, although numerous, violent actions in comedies were less serious, less explicit, and less likely to be intentional. Dramas tended to depict less serious violent actions and lesser injury severities, but their violent actions tended to be more explicit and were more likely to be intentional.

This study is limited by several factors, including its sampling, its scoring methods, and its choice not to assess psychological or behavioral sequelae for viewers of the violent scenes. Because the sample represents the most widely seen movies of 1994 and is characteristic of the American film industry at the end of the 20th century, generalizability is good. The scaling was intentionally simple, although it may have led to oversimplification of especially complex scenes. Psychological consequences for the film characters—initiator, recipient, bystander—involved in the violence were assessed during coding but not included in this article. No attempt was made with these 100 films, however, to assess audience reactions. We also did not distinguish in judgmental terms between films with differing violent profiles.

Table 3 *Injury severity by seriousness of violent action**

Seriousness	Injury severity Mild	Severe	Critical	Injury not shown	Total no.
Minimal	1 (0)	1 (0)	2 (0.1)	400 (18.3)	404
Moderate	33 (1.5)	14 (0.6)	1 (0)	769 (35.2)	817
Lethal	11 (0.5)	40 (1.8)	115 (5.3)	797 (36.5)	963
Total	45 (2.1)	55 (2.5)	118 (5.4)	1,966 (90.0)	2,84

*Data are given as number (percentage) except as noted.

Violence has always been a part of American movies, starting from the first film to be distributed widely, *The Great Train Robbery*, which contained an optional reel of gunplay left to the discretion of the local projectionist. Glucksmann cited figures from the 1930s in which 45 murders and more than 400 crimes were depicted in 115 separate crime films, and from the 1950s in which more than 650 crimes or acts of violence were identified in 100 selected films from that era.[6] But for years, the Hays Production Code kept the appearance of criminal violence, sex, vulgar language, and obscenity below a strict threshold. Since the code was retired in 1968, a much less stringently defined rating process under the aegis of the Motion Picture Association of America has been used.[7] This voluntary system is often the sole hurdle outside the production company an American movie must pass over before entering the marketplace. Standards for presenting violence in movies continue to evolve; a complex interlocking set of additional forces for change has also included the increasing number of entertainment outlets other than the movies, growing competition within the movie industry, and emphasis on international marketing—as well as attendant demands for less talk, more action.

Critics have commented that the use of extreme violence by many in the current generation of filmmakers means that, by repetition and overfamiliarity, violence is

Table 4 *Odds ratios and 95% confidence intervals for 3 principal genres by violence characteristic*

Violence characteristic	Genre Action	Comedy	Drama
Seriousness	1.24 (1.08-1.42)	0.80 (0.69-0.92)	0.84 (0.71-1.00)
Explicitness	1.46 (1.26-1.69)	0.56 (0.47-0.67)	1.42 (1.19-1.70)
Injury severity	0.84 (0.70-1.01)	1.18 (0.98-1.41)	0.89 (0.73-1.08)
Consequences	0.82 (0.60-1.13)	1.09 (0.81-1.46)	1.34 (0.99-1.83)
Intentionality	2.42 (1.66-3.54)	0.40 (0.30-0.55)	1.63 (1.05-2.52)

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Violence that should lead to massive injury does not in most scenes of *True Lies*

no longer as fraught with meaning as it once was. Violence may be used to move the film's story forward with conflict and narrative structure in place of more difficult tasks involving the development of story and character. Stephen Prince, a leading film critic, points out[8(p11)]:

> Graphic violence is now embedded in contemporary cinema as a formulaic element, endlessly repeated, and often removed from any recognizably human context. It solves story problems by providing talented as well as mediocre filmmakers with an easily-assembled, if mechanical, narrative structure. It also substitutes for thought and reflection.

Central to issues of art, style, and storytelling, however, is the possibility that violence serves as an opportunity for the filmmaker, as noted by Lewis Cole, chair of the Film Division of Columbia University's School of the Arts: "The moment when rationality fails and a character throws him- or herself into action is a crucial option for a dramatist. The realistic portrayal of violence is one of the distinguishing marks of great artists."[9]

The results of this study suggest 3 separate considerations. The first is that, through the appearance of violence against persons across all film genres, a message is being conveyed that such violence deserves to be watched. The huge gross from violent films shows that consumers around the globe support this notion. To meet public demand for their product, screenwriters and filmmakers continue making movies that portray violent actions.

The second consideration is that high levels of violence, whether intentional or unintentional, over time seem to become acceptable—perhaps even expected by the modern viewing audience. (Violent scenes in films from earlier eras now often appear as if they "wore the soft gloves of much gentler conventions"[10]; future generations may say the same about violence in today's films.) Viewers of contemporary movies may, indeed, recognize that a given violent act against another human would not necessarily occur in the way it is shown on film. The professional specialties of stunt double, fight choreographer, and special effects coordinator are dedicated, however, to convincing movie audiences to believe otherwise.

The third consideration addresses public health and injury prevention education, in particular: through de-

emphasis of injury consequences in the movies, many times the intentionally violent actions by 1 person against another appear to have no injurious outcomes. Once over a certain threshold, however, when the violent action is exaggerated to a high degree, the consequences to the recipient of that action are shown as lethal. This dichotomy depicts only fragments of the relationship between violent actions and consequent injuries and may become problematic if it succeeds in misleading viewers about the nature and extent of injuries that might accompany performance of all but the most violent of violent acts.

Public health will probably not be advanced by attempting to convince the film industry to soften the appearance or diminish the intensity of movie scenes that include violence against persons. But, paralleling the efforts to persuade moviemakers to reduce the number of actors shown smoking cigarettes and increase the visibility of seat-belt use, it may be time for the public health community to express its opinion about the use of violence against persons with misleading portrayals of injury consequences.

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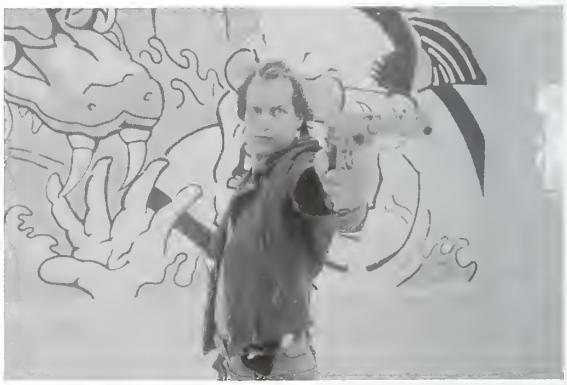

Kobal Collection

Throughout *Natural Born Killers,* characters escape injury despite lethal violence

COMMENTARY

The mind sees more than the movie frame

The paper by McArthur and colleagues is interesting, provocative, and fun to read. The authors analyzed and coded the actions in the top 100 movies of 1994, ranked by money earned as a proxy for the number of people who saw the film. It is unclear, however, whether this study is science or literary criticism, but perhaps it doesn't matter.

The authors use their statistical analysis to make several points, including that movies show a huge amount of violence. They suggest that film violence is unrealistic in that it does not show the physical consequences of the violent acts: the blood and gore of tissue destruction. I don't know why this point needs a statistical analysis, unless their aim is to use the statistics to advocate against violence in the movies.

I also question their argument. Does the absence of blood and gore really make the violence less convincing? What if we applied this standard to Shakespeare, or to the old Bergman movie *The Virgin Spring (Svensk Filmindustri)*. If my memory serves me well, there was only one violent act—the rape and murder—with little physical evidence. But that movie had a more powerful and lasting impression on me than all the silliness of the westerns or the *Star Wars* (Lucasfilm) movies. Brilliant writers and directors can elicit powerful emotional responses without resorting to anatomic realism.

There is more to addressing this issue of the effects of film violence than simply advocating that movie directors show the consequences of violent acts. There is more to understanding human nature than counting the events. This paper misses something about the nature of human perception; the mind sees more than the movie frame.

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Development of a telemedicine program

A review of 1,000 videoconferencing consultations

ABSTRACT **Objective** To examine the financial and organizational characteristics, demand for services, and satisfaction outcomes of a growing telemedicine program serving both urban or suburban and rural populations. **Design** Retrospective review of 1,000 consecutive telemedicine consultations in the University of California (UC) Davis Telemedicine Program. **Setting** Telemedicine videoconferencing units, used to integrate care in the UC Davis Health System among the UC Davis Medical Center and several urban or suburban primary care clinics, rural hospitals, and clinic affiliates. **Subjects** A total of 657 consecutive patients who consented to a telemedicine consultation. **Main outcome measures** Demographic information about the patient population, the rural and urban or suburban clinics, the types of specialty consultations, and telemedicine equipment used in the UC Davis Health System. Patient and physician satisfaction were measured on a 5-point Likert scale. **Results** Patients and primary care physicians reported high levels of satisfaction. Rural clinics requested more and a greater variety of specialist consultations than urban or suburban clinics. **Conclusion** Although referring physicians and patients indicate a high level of satisfaction with telemedicine services and insurers are negotiating reimbursement policies, additional research must investigate the reasons why some payers, patients, and providers resist participation in these services.

INTRODUCTION

A driving force behind the growth and development of telemedicine programs across the country has been the need to increase access to medical services in rural settings. Telemedicine enhances the quality of local care[1] and patient satisfaction[2] by allowing patients to see specialist physicians in their home communities, rather than expending time and money traveling to large urban centers.

Since the mid-1990s, the cost of technology has rapidly decreased,[3] making videoconferencing affordable to more health care recipients. In 1996, the Office of Rural Health Policy conducted an interview of rural hospitals to assess their use of telemedicine.[4,5] Of the 2,472 hospitals surveyed, 499 used telemedicine. Of these, a third had used videoconferencing for a variety of clinical services. In fact, cardiologic, dermatologic, and psychiatric services were used at least once by more than 30% of facilities.

In 1996, the University of California (UC) Davis Health System began a telemedicine pilot at 3 sites within its primary care network comprising urban and suburban clinics owned by the university. The use of telemedicine in the primary care network became the prototype for tele-

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medicine applications in a variety of rural hospitals and correctional facilities, both of which have had problems with health care access.

We review the start-up experience of a telemedicine program based in a large regional health system in northern California. We reviewed 1,000 consultations to assess demographic characteristics of patients and physicians and service provision in the program. We also assessed patient and primary care physician satisfaction. In our analysis, we compared the performance, demand, and satisfaction scores of rural and urban or suburban clinics.

PARTICIPANTS AND METHODS

The study population included 657 patients who were seen during the course of 1,000 telemedicine consultations (some were seen for follow-up). Patients were asked by their physician about receiving specialist care through a telemedicine consultation. Participation in telemedicine was voluntary for both patients and physicians. Patients could choose to see the physician in person or by telemedicine.

On the day of the appointment, after signing an informed consent agreement, patients were briefed on the nature of the telemedicine consultation, including who would be involved and the patient's right to change the mode of care to face-to-face consultation. Patients who were younger than 18 years required the consent of a parent or legal guardian to participate in the telemedicine consultation. In cases of medical emergency—such as acute myocardial infarction or suicidal ideation—patients were referred to local medical services in lieu of telemedicine. Patient demographic information and insurance status—commercial insurance, Medicare, Medi-Cal (California's Medicaid), or grant support—were recorded for all consultations.

PROCEDURES

Physicians desiring specialty consultation for their patients had the option of offering telemedicine rather than traditional consultations. Patients willing to be seen by a specialist by videoconference were scheduled for an appointment at the nearest telemedicine clinic affiliated with their primary care physician's office. A medical assistant at the primary care site arranged the consultation and faxed relevant patient history and physical examination data to the UC Davis Telemedicine Program, which forwarded the information to the specialist consultant before the consultation.

Following the consultation, patients rated their satisfaction on a 1-page questionnaire containing 5-point Likert-type items (5 = excellent). Respondents rated their ability to speak freely with their consultant, their willingness to use telemedicine in the future, the competence of the staff to handle the telemedicine equipment (ability to troubleshoot technical difficulties and to optimize audio and video capabilities), the ability of the telemedicine consultation to meet their medical needs, and overall satisfaction. The patient satisfaction form was faxed to the UC Davis Telemedicine Program and stored in secured data files. All reports of these data have been tabulated in summary form.

Primary care physicians were invited to participate in the consultation and rated their satisfaction with the experience on a 5-point Likert scale. Physicians responded to questions about their ability to understand the specialist consultant, the quality of the audio and video transmission, performing physical examinations with the aid of the specialist consultant (such as using the nasolaryngoscope), and overall satisfaction. All responses were confidential.

RESULTS

Response rates

Although refusal rates were not tracked for all patient groups, a high percentage of patients were willing to use telemedicine for consultation. Even in the area of psychiatric care, where acceptance rates for telemedicine were expected to be low, 29% of patients chose telemedicine for the initial visit, whereas 35% chose telemedicine for follow-up care. These results may not be representative of all specialty clinics provided by telemedicine.

Demand for services

The first 1,000 consultations mainly included patients seen in 6 urban or suburban clinics and 2 rural clinics. The 606 (excluding 51 patients seen in correctional facilities) patients who used telemedicine in a rural or suburban location differed significantly in age ($P<0.05$). The rural telemedicine patients had a larger proportion of pediatric patients (17.9% vs 7.3%) than the urban or suburban group. There was not a statistically significant difference between the proportion of male and female patients seen in the rural and suburban clinics ($P = 0.13$). For rural and suburban or urban clinics, cancellation rates were 10.8% and 11.5%, respectively ($P = 0.75$).

Rural and urban or suburban primary care clinics were compared in several variables using t tests (table 1). The mean distance of the rural and urban or suburban clinics was 123.25 and 40.8 miles, respectively, from UC Davis Medical Center ($t = 3.55$, $P<0.05$). Rural clinics used more consultants (18 vs 7; $t = 2.38$, $P = 0.05$) and more medical specialties for consultations (13.5 vs 5; $t = 2.84$, $P<0.05$) than urban or suburban clinics.

Telemedicine consultations were provided in 19 different specialty areas. Overall, the most common telemedicine consultations requested were nutrition, mainly for diabetic and lipid disorders (32.8%); dermatology (22.3%); and behavioral health, psychiatry, or both (15.8%) (table 3). Of the 1,000 consultations, 65.8%

Table 1 *Clinic characteristics of first 1,000 telemedicine consultations at UC Davis Health System, 1996-1999*

Location	Distance from medical center, mi	Travel time to medical center, hr:min	Consultants, No.	Specialties (total No.)
Clinic				
Auburn	36.7	0:53	3	Dermatology, psychiatry (2)
Chico	93.3	2:38	13	Cardiology, dermatology, otolaryngology, pain management, endocrinology, gastroenterology, orthopedics, podiatry, psychiatry, rheumatology (10)
Davis	21.9	0:32	3	Dermatology, psychiatry (2)
Placerville	37.9	0:52	7	Dermatology, otolaryngology, infectious disease, nutrition, psychiatry (5)
Quincy	148.2	4:16	13	Cardiology, dermatology, otolaryngology, endocrinology, genetics, nephrology, nutrition, orthopedics, psychiatry, rheumatology, surgery (11)
Roseville	20	0:31	2	Dermatology, psychiatry (2)
Sonora	98.3	2:41	23	Dermatology, otolaryngology, endocrinology, gastroenterology, genetics, hematology, hepatology, infectious disease, nutrition, obstetrics-gynecology, orthopedics, pain management, podiatry, psychiatry, rheumatology, urology (16)
Vacaville	35	0:52	14	Cardiology, dermatology, otolaryngology, endocrinology, infectious disease, nutrition, orthopedics, pain management, psychiatry (9)
Correctional facilities*	≤355.5	≤5:55	8	Dermatology, otolaryngology, infectious disease, orthopedics, endocrinology (5)

*Correctional facilities were located in both Sacramento and Crescent City.

were initial evaluations and 34.1% were referrals for follow-up appointments. The overall cancellation rate was 11.1%, with a range from 21.4% (infectious diseases) to 0% (rheumatology). Specialties involving unique examination procedures or imaging techniques (otolaryngology, dermatology, and orthopedics) generally required 30 minutes or less of consultation time for initial and follow-up visits. Interview-based consultations, including those provided in nutrition, behavioral health, and endocrinology, required as much as 60 minutes for the initial evaluation and 30 minutes for follow-up appointments.

Satisfaction

Data regarding patient satisfaction were collected on 362 of the 1,000 consultations (table 4). Interview-based specialties (such as endocrinology) were more highly rated by patients than those involving the use of scopes, cameras, or specialized examinations (such as dermatology or orthopedics).

Table 2 *Specialty characteristics of first 1,000 telemedicine consultations* at UC Davis, 1996–1999*

Specialty	Visits, No.	Follow-up visits, No.	Total volume, %	Cancellation rate, %	Time for initial visit, min	Time for follow-up visit, min
Nutrition	172	156	32.8	16.3	60	30
Dermatology	158	65	22.3	9.0	15	15
Behavioral health	85	73	15.8	7.3	50	25
Otolaryngology	65	5	7.0	8.2	30	30
Orthopedics	66	3	6.9	5.9	30	15
Endocrinology	44	15	5.9	13.2	60	30
Rheumatology	21	9	3.0	0	60	30
Pain management	16	6	2.2	18.5	60	30
Infectious disease	8	3	1.1	21.4	60	30

*Specialties with ≤5 consultations, including cardiology, gastroenterology, genetics, hematology, hepatology, nephrology, obstetrics-gynecology, podiatry, surgery, and urology, were excluded from this analysis (2.8% of total volume).

Table 3 *Characteristics of consultations conducted in suburban or urban versus rural telemedicine network**

Characteristic	Suburban-urban, No. (%) (N = 717)	Rural, No. (%) (N = 223)
Time period†		
Jul 1996-Jan 1997	11 (1.5)	0 (0)
Jan 1997-Jul 1997	58 (8.1)	0 (0)
Jul 1997-Jan 1998	154 (21.5)	0 (0)
Jan 1998-Jul 1998	202 (28.2)	44 (19.7)
Jul 1998-Feb 1999	292 (40.7)	179 (80.3)
Consultation type‡		
Initial visit	466 (65.0)	140 (62.8)
Follow-up	251 (35.0)	83 (37.2)
Insurance type†		
Medi-Cal	7 (1.0)	118 (52.9)
Medicare	76 (10.6)	8 (3.6)
Indigent	0 (0)	2 (0.9)
Self-pay	2 (0.3)	0 (0)
Managed care	627 (87.4)	92 (41.3)
Other	5 (0.7)	3 (1.3)

*Sixty consultations were not classified as either suburban-urban or rural.
†$P < 0.05$.
‡$P = 0.96$.

A total of 204 primary care physicians, representing only the rural clinics, completed satisfaction surveys (table 5). Primary care physicians rated their overall satisfaction with telemedicine at 4.30 or greater. Their satisfaction with the examination process and the quality of the audio and video transmission fell below 4.00 in only 1 clinical area: rheumatology. In about 1 of 5 consultations, the physician reported a technical difficulty. Commonly reported problems were lag time between the audio and video signals, unexpected disconnections, "choppy" audio transmission, and difficulty manipulating the peripheral devices to acquire a clinically acceptable image.

Reimbursement and program costs

The method of payment was recorded for each telemedicine consultation provided (table 3). Direct costs of the services were not measured.

The type of insurance coverage showed significant differences between the rural and suburban or urban populations of telemedicine patients ($P<0.05$). The rural consultations were more frequently billed to Medi-Cal (52.9% vs 1.0%) and fewer consultations through commercial insurance (41.3% vs 87.4%) than the urban or suburban population. Insurance coverage through Medicare was 3 times less common in the rural population than in the urban or suburban population (3.6% vs 10.6%).

The total average cost of videoconferencing units is $12,800. Peripheral devices, such as a dermatology camera and a nasopharyngoscope, with its own light source and camera, may reach $19,000 in system costs. Variable costs for telemedicine relate to telecommunications line charges—which can be as much as $60 per hour for digital phone service connection—and clinic coordination. These costs would not be incurred in a typical face-to-face clinic.

DISCUSSION

The results from this project suggest differences in demand for specialty services between rural and suburban sites, with rural sites having higher demand overall, and in the breadth of specialties. We found high satisfaction with telemedicine consultations among both patients and pri-

Table 4 *Patient mean satisfaction scores* for the first 1,000 telemedicine consultations at UC Davis, 1996-1999 (n = 362)*

Specialty	Ability to talk freely	95% CI	Ability to meet medical needs	95% CI	Staff well trained	95% CI	Will use in future	95% CI
Nutrition	4.68	4.51-4.85	4.33	†	4.72	4.55-4.89	4.60	4.39-4.81
Dermatology	4.57	4.45-4.69	4.63	4.52-4.74	4.64	4.52-4.76	4.79	4.65-4.93
Behavioral health	4.59	4.38-4.80	4.05	3.61-4.49	4.66	4.48-4.84	4.63	4.35-4.91
Otolaryngology	4.76	4.55-4.97	4.63	†	4.59	4.38-4.80	4.86	4.78-4.94
Orthopedics	4.48	4.24-4.72	4.29	†	4.29	4.12-4.46	4.88	†
Endocrinology	4.77	4.59-4.95	4.87	4.75-4.99	4.87	4.75-4.99	5.00	†
Rheumatology	4.42	4.15-4.69	4.42	4.17-4.67	4.65	4.43-4.87	4.92	†
Pain management	4.85	†	4.77	†	4.92	†	5.00	†
Other‡	4.36	4.04-4.68	4.52	4.20-4.84	4.57	4.31-4.83	4.68	4.39-4.97
All specialties	4.59	4.52-4.66	4.57	4.48-4.66	4.68	4.62-4.74	4.79	4.72-4.86

CI = confidence interval.
*Mean scores are derived from a 5-point Likert-type questionnaire (5 = excellent).
†Number of patients is too small to reliably calculate 95% CI.
‡Other includes cardiology, gastroenterology, genetics, hematology, hepatology, infectious disease, nephrology, podiatry, pediatrics, perinatology, and urology.

AP/Walt Frerck

This physician, treating a boy with burns in a remote Texas hospital, is transmitting live video images of the burn to a specialist 250 miles away

mary care physicians. Participation in telemedicine was completely voluntary. Therefore, the results presented in this article may not be representative of all physicians' and patients' willingness to use this modality of care.

The use of telemedicine may result in increased medical interventions among the patients who use it. This is because it is being introduced to patient groups (Medi-Cal recipients) who before the availability of telemedicine had limited access to specialist services. The extent to which health service use has increased because of telemedicine cannot be stated at this time. Once data are collected on health service use resulting from telemedicine, research can be focused on changes in morbidity and mortality among telemedicine patients and possibly reducing overall health care costs.

Other concerns about telemedicine relate to the effect it may have in eroding the involvement of primary care physicians in the care of their patients. This program has found that many primary care providers, in fact, derive an educational benefit from collaborating with a physician specialist. Within our first 1,000 consultations, telemedicine referrals from primary care physicians were generated because of the limited access to medical specialists in rural communities. In the past year, this program has observed that midlevel providers—physician assistants and nurse practitioners—are increasingly referring patients to telemedicine in communities where there is a shortage of primary care physicians.

Barriers to the use of telemedicine include the problem of reimbursement. In California, a law was passed in 1996 that mandated reimbursement for telemedicine services.[6] Nonetheless, many insurance payers have not developed a reimbursement policy for telemedicine and have required education about the clinical content of the standard telemedicine visit, the role of the presenting provider, and the importance of paying for the resources involved in care, mainly telecommunications costs. Medi-Cal is currently evaluating the effect of telemedicine in traditionally underserved areas and the financial effects on the state of providing payment.

At the national level, the Health Care Financing Administration has established policy mandating, as of January 1999, that Medicare reimburse for telemedicine in underserved rural areas when the referring practitioner is present. This policy, however, had little effect on the first 1,000 telemedicine consultations provided at UC Davis.

There are several limitations to the data presented in this report. First, the patients, referring physicians, consultants, and health system in this study may not be generalizable to other settings. Furthermore, diagnostic data were not collected, and there were no clinical outcome measures, only subjective ratings of satisfaction. Data on objective medical outcomes will be important to evaluate in the future because there may be diagnoses that are less amenable to treatment by telemedicine consultation. Second, the satisfaction data are limited because, owing to the lack of a telemedicine coordinator in most clinic settings,

Table 5 *Rural provider satisfaction scores* for the first 1,000 telemedicine consultations at UC Davis, 1996–1999 (N = 204)*

Specialty	Ability to understand specialist	95% CI	Ability to perform examination	95% CI	Audio quality	95% CI	Video quality	95% CI
Dermatology	4.74	4.64–4.84	4.50	4.34–4.66	4.55	4.41–4.69	4.59	4.46–4.7
Endocrinology	4.79	4.64–4.94	4.65	4.42–4.88	4.07	3.57–4.57	4.52	4.22–4.8
Pain management	4.86	†	4.50	†	4.50	†	4.79	†
Rheumatology	4.82	4.64–5.00	3.93	3.50–4.36	3.96	3.60–4.32	3.75	3.27–4.2
Other‡	4.73	4.53–4.93	4.67	4.45–4.89	4.05	3.69–4.59	4.61	4.39–4.8
All specialties	4.76	4.53–4.83	4.46	4.34–4.58	4.30	4.17–4.43	4.48	4.37–4.5

CI = confidence interval.
*Mean scores are derived from a 5-point Likert-type questionnaire (5 = excellent).
†Number of providers is too small to reliably calculate 95% CI.
‡Other includes behavioral health, nutrition, gastroenterology, genetics, hematology, hepatology, infectious disease, nephrology, orthopedics, otolaryngology, pediatrics, perinatology, podiatry, and urology.

the questionnaire was not administered to every patient. In addition, there was no control group against which to compare any ratings, and the study was nonrandomized. To that end, 2 randomized controlled trials have been initiated in the past year on the delivery of home health and psychiatry through telemedicine compared with traditional face-to-face care.

Despite these limitations, these data provide important information from a usual-care perspective for those who are considering telemedicine services to provide specialty care. In the future, controlled studies are needed to further assess the effects of telemedicine on patient outcomes and cost-effectiveness.

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COMMENTARY

What do we know about telemedicine, and what will it mean for primary care physicians?

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In the early 1990s, it was the exception rather than the rule to encounter a physician who was familiar with telemedicine.[1] Today, most physicians are aware of it and many have strong opinions about its potential. Traditionally, telemedicine is the term used to explain the delivery of any type of health service or education via telecommunication technologies, typically as videoconferencing. In the first and second waves of telemedicine, from 1960 to 1985 and from 1990 to 1998, respectively, the majority of clinical activity was provided in specialty areas, such as mental health and cardiology.[2]

Research studies to assess satisfaction with telemedicine, conducted during the two waves, yielded uniformly consistent results. A systematic review of studies of video-based telemedicine showed that all studies reported high levels of patient satisfaction.[3] This review also pointed to serious flaws in these research efforts, however, including small sample sizes and other weaknesses in study design. These flaws limit the validity and generalizability of the studies. Of the published studies, only 22% (7/32) included 100 or more patients, with 32% (10/32) including less than 20 patients. In 88% (28/32), criteria regarding patient selection were not specified. Many studies failed to specify the methodologies used for assessing satisfaction. The survey design was often problematic, such as using multiple constructs in a single question.

The results of this review do not mean that telemedicine itself is flawed. They suggest that patient satisfaction is still unproven. A bigger question than the quality of research to date[4] is whether the results from a specific telemedicine project can actually be generalized across all telemedicine contexts.

Researchers in the health communications field have often found a disparity between the positive results of satisfaction surveys and what patients truly believe about consultations with health care professionals.[5] Even though most patients surveyed report satisfaction, they generally report dissatisfaction with the communication accompanying their medical care.[6-8] In-depth research has showed the importance of communicative and contextual variables, such as providers' interpersonal skills, lack of communication with patients and their families, or the use of technical jargon. The bottom line is that providing health is a complex phenomenon and its context is important. Therefore, it may be an oversimplification to merely ask people if they are satisfied with telemedicine. Instead, it may be more important to understand the context in which care is being provided—whether it is in the primary care physician's office, the patient's home, or the hospital—and then link the best telemedicine practices to the situation at hand.

Just as we acknowledge how little we really know about patient or provider satisfaction with telemedicine, we find ourselves evolving into the third wave of telemedicine, from 1999 to the present. Language is all-important in the current wave, and the word "telehealth" is emerging as the de facto description of the new phenomenon. The Internet, and the emergence of "e-health," offers novel kinds of health services and information. Although still in its infancy, e-health not only opens up a new form of universal access, it also drives home the irrelevance of health services requiring a synchronous or real-time form of delivery.

Whatever forms of telemedicine ultimately dominate, there is little doubt that they will somehow impact the practice of primary care medicine. At a minimum, these technologies will facilitate the ability of a primary care physician to link patients with specialists. Currently, this

practice is used mostly by rural generalists who are able to link their patients electronically with an urban specialist. Changes in licensure, however, could enable a primary care physician to arrange a consultation with the first available specialist, regardless of location.

Telemedicine may enable advanced practice nurses and physician assistants to provide primary care in remote locations.[9] It is unlikely that such care would replace that provided by primary care physicians, but it is possible that enhanced monitoring and mentoring through the use of telemedicine technologies could boost the role of these professionals. A handful of physicians are already enjoying the benefits of communicating with their patients asynchronously, at convenient times, by e-mail. Advances in telemonitoring devices may enable a patient to transmit vital information to the database of their primary care physician, thus alerting him or her to data that fall outside of normal boundaries. Finally, Internet videoconferencing technologies may allow doctors to offer convenient "house calls."

In many ways, primary care physicians will drive the development and application of telemedicine technology. Because they are gatekeepers to so many health services in the United States, the future of much of telemedicine lies in their hands. Telemedicine will not replace them; it will simply assist them.

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Achieving further glycemic control in type 2 diabetes mellitus

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ABSTRACT **Objectives** To identify patients with type 2 diabetes mellitus who were in poor glycemic control and therapeutic adjustments that might improve control. **Design** Using electronic pharmacy data, we assigned subjects to 1 of 4 therapeutic categories. We then identified patients within each category who did not meet the recommended standard of glycemic control (glycosylated hemoglobin [Hb A_{1c}] <0.08 [<8.0%]) and studied their therapeutic regimens for possible improvements. **Subjects** The subjects were 5,061 members of a large group-model health maintenance organization who had type 2 diabetes and 12 months of 1997 health plan eligibility. **Main outcome measures** The dosage of antihyperglycemic agents (sulfonylureas, metformin, and insulin) in relation to glycemic control as measured by the Hb A_{1c}. **Results** A significant number (n = 1,570 [31.0%]) of persons with type 2 diabetes might improve their glycemic control with simple adjustments to their pharmacologic therapy. **Conclusion** Busy clinicians with heavy workloads can improve their management of diabetes by identifying patients whose glycemic control could be improved through a change in medication or simple adjustment in dosage.

INTRODUCTION

Accumulating evidence demonstrating the benefits of intensive diabetes care[1,2] has put health care plans and clinicians under increasing pressure to improve the glycemic control of patients with diabetes.[3-6] The recent addition of metformin, acarbose, rosiglitazone, and pioglitazone to the therapeutic armamentarium provide more options for patients who have not achieved adequate glycemic control with the use of sulfonylureas or insulin alone. Yet, many patients still do not have satisfactory glycemic control, including patients whose health care organizations meet or exceed national standards of care. Kaiser Permanente Northwest's initiative to provide comprehensive care for patients with type 2 diabetes mellitus, including expanded case management, enhanced health education, and aggressive testing of glycemic control, has been described else-

where.[7] In this report, we identify opportunities for further improvement in glycemic control, with specific focus on the therapeutic regimens currently in use.

PARTICIPANTS AND METHODS

The subjects of this study were members of a long-established, not-for-profit, group-model health maintenance organization, Kaiser Permanente Northwest Division. Its diabetes registry has been detailed elsewhere.[8] For this study, we selected 6,287 members in the diabetes registry who responded to a 1997 survey and who had 12 months of health plan eligibility in 1997. From these, we excluded 454 members who had type 1 diabetes mellitus and 582 members who did not have an Hb A_{1c} measurement in 1997. We also excluded 173 members who received 3 or more antidiabetic drugs in 1997 (because their therapeutic regimen was likely in flux, proper assignment to a therapeutic category could not be assured). Finally, because of concerns about sample size, we excluded 17 members who received only acarbose or troglitazone. These exclusions yielded a final study population of 5,061.

Using electronic pharmacy data maintained by Kaiser Permanente Northwest, we assigned subjects to 1 of 4 therapy categories: users of insulin, alone or in combination with metformin or sulfonylureas; users of metformin, alone or in combination with sulfonylureas; users of sulfonylureas only; and persons taking no antidiabetic drug. For comparability, prescription fills of sulfonylurea were converted into glyburide equivalents using maximum doses described by Gerich.[9] Within these groups, we divided patients into those who met or exceeded a recommended standard of glycemic control (Hb A_{1c} <0.08 [<8.0%]) and those who did not (≥0.08 [≥8.0%]).

RESULTS

Glycemic control within the study population was good overall. The mean (SD) Hb A_{1c} level was 0.076 (0.013). Almost two thirds (66.3% [n = 3,356]) of the cohort had a mean Hb A_{1c} level below 0.08, and 87.3% (n = 4,416) were below 0.09.

The mean age of the study population was 65.1 years, 49.9% (n = 2,525) were women, and the average duration of diabetes was 10 years. The mean body mass index (calculated as weight in kilograms divided by the square of height in meters) was 31.1. Users of insulin alone or in combination with sulfonylureas or metformin (n = 1,346) made up 26.6% of the study population. Users of metformin alone or in combination with sulfonylureas were 15.3% of the total population (n = 772). Users of sulfonylureas as monotherapy constituted the largest proportion (40.6% [n = 2,054]) of the study population, and 17.6% of the population was taking no antidiabetic drugs (n = 889).

In table 1, we divide the sulfonylurea-only users into 2 levels of control (±0.08) and compare them with subjects using no drugs. Of the 2,054 sulfonylurea-only users, 1,385 (67.4%) had mean Hb A_{1c} values below 0.08. Compared with sulfonylurea-only users with Hb A_{1c} levels of 0.08 or above (n = 669), these better-controlled sulfonylurea-only users were older (P<0.001), more obese (P<0.01), and more likely to be women (P<0.001). The sulfonylurea-only users with Hb A_{1c} levels below 0.08 also

Table 1 *Patient characteristics, sulfonylurea-only users, and patients receiving no drug therapy**

Characteristics	No drug therapy	Sulfonylureas only Hb A_{1c} ≥0.08	Sulfonylureas only Hb A_{1c} <0.08	Total
Study subjects, no.	889	669	1,385	2,054
Mean Hb A_{1c} level†	0.07	0.09	0.069	0.076
Age, yr‡	65.1	63.8	66.0	65.3
Sex, female, No. (%)	459 (51.6)	306 (45.7)	669 (48.3)	975 (47.5)
Race, white, No. (%)	834 (93.8)	593 (88.6)	1,285 (92.8)	1,878 (91.4)
BMI§	30.2	30.5	31.3	31.0
Years since diabetes mellitus recognized	7.8	7.8	7.2	7.4
1997 daily glyburide equivalents, mg‡	—	13.0	9.7	10.8
Years taking drug§	—	4.2	3.8	3.9
1997 prescription fills of sulfonylureas†	—	5.8	4.6	5.0

BMI = body mass index.
*Except as otherwise noted, data are mean values. Statistical comparisons are made between sulfonylurea users with glycosylated hemoglobin (Hb A_{1c}) levels of 0.08 or higher (≥8.0%) and those with Hb A_{1c} levels below 0.08 only.
†Expressed as a proportion of 1. For conventional units, multiply by 100 to obtain percentage.
‡P< 0.001.
§P< 0.01.

had had diabetes for a slightly shorter time ($P<0.1$). The mean daily dose of sulfonylureas (in glyburide equivalents) for those with Hb A_{1c} levels below 0.08 was much lower than for those above this threshold ($P<0.001$). Well-controlled sulfonylurea-only users had been taking sulfonylureas for a shorter time and received fewer prescription fills of sulfonylureas than those with Hb A_{1c} levels of 0.08 or above ($P<0.001$ for both).

Table 2 displays similarly organized statistics for insulin users with Hb A_{1c} values below 0.08 (n = 783 [58.2% of insulin users]), those with values of 0.08 or above taking less than 100 units of insulin per day (n = 393 [29.2%]), and those with Hb A_{1c} values of 0.08 or above taking 100 units or more of insulin per day (n = 170 [12.6%]). Users of insulin with Hb A_{1c} levels below 0.08 were much more likely to be women ($P<0.001$) than were either of the groups with Hb A_{1c} levels of 0.08 or above. Users of insulin who had Hb A_{1c} levels above 0.08 and who were receiving more than 100 units of insulin per day were more than 4 years younger ($P<0.001$). Finally, those with Hb A_{1c} levels of 0.08 or above receiving fewer than 100 units of insulin per day had had diabetes significantly longer ($P<0.001$) than those receiving more than 100 units or those with Hb A_{1c} levels below 0.08.

We also divided the subjects receiving metformin into 3 groups (table 3): those with Hb A_{1c} values below 0.08 (n = 434 [56.2%]), those with Hb A_{1c} values of 0.08 or above receiving 1,500 mg or more of metformin per day (n = 233 [30.2%]), and those with Hb A_{1c} values of 0.08 or above receiving less than 1,500 mg per day (n = 105 [13.6%]). Well-controlled users were somewhat more likely to be women than were users with Hb A_{1c} levels of 0.08 or above who were receiving low doses of metformin (46.7%) and those with Hb A_{1c} levels of 0.08 or above who were high-dose users (36.9%), and they were more likely than either of the other 2 groups to be white ($P<0.05$). High-dose users with Hb A_{1c} values of 0.08 or above also were significantly younger ($P<0.01$) than those with values below 0.08 and had had diabetes longer ($P<0.01$). Low-dose users with Hb A_{1c} levels of 0.08 or above had been taking metformin for less time ($P<0.001$) and received fewer prescription fills of the drug ($P<0.05$).

DISCUSSION

Some demographic patterns emerged that may assist health plans and physicians in identifying at-risk patients. Most notably, younger patients who had type 2 diabetes longer were in poorer control than older patients who had type 2 diabetes for shorter duration. This finding, and the finding that women were in better control than men, holds across all drug therapy categories.

Despite the good overall level of glycemic control in this health plan, we found room for improvement. Of 5,061 members in this study, 1,570 (31%) had Hb A_{1c} values that exceeded the American Diabetes Association's recommended threshold for action (0.08).[10] Many of these members could benefit from relatively simple adjustments to their therapeutic regimens.

First, almost a third (n = 669) of the 2,054 patients (32.6%) receiving sulfonylurea monotherapy had an Hb A_{1c} of 0.08 or above. They had been taking sulfonylureas somewhat longer and were receiving higher doses and

Table 2 *Patient characteristics, users of insulin alone or with any oral agent**

Characteristics	Hb A_{1c} ≥0.08 Insulin, ≥100 U/day	Hb A_{1c} ≥0.08 Insulin, <100 U/day	Hb A_{1c} < 0.08	Total
Study subjects, no.	170	393	783	1,346
Mean Hb A_{1c} level†	9.0†	9.0†	6.9‡	7.8
Age, yr	62.2†	66.1‡	66.9‡	66.1
Sex, female, no. (%)	83 (48.8)†	190 (48.3)†	456 (58.2)‡	729 (54.2)
Race, white, no. (%)	160 (94.1)	337 (85.7)	730 (93.2)	1,255 (93.2)
BMI	33.1†	28.9‡	32.2§	31.4
Years since diabetes mellitus recognized	15.0†	17.9‡	15.2†	16.0
1997 average daily insulin dose, units	164†	60‡	99§	96
Years taking drug	5.2	5.4	5.3	5.3
1997 prescription fills of insulin	9.7	10.3	10.2	10.2

Hb A_{1c} = glycosylated hemoglobin (hemoglobin A_{1c}); BMI = body mass index.
*Except where otherwise noted, data are mean values. Figures with different symbols (†, ‡, and §) are significantly different from each other ($P<0.05$).
†Expressed as a proportion of 1. For conventional units, multiply by 100 to obtain percentage.

Table 3 *Patient characteristics and users of metformin alone or with sulfonylureas**

Characteristics	Hb A_{1c} ≥0.08 Metformin dose ≥1,500 mg/day	Hb A_{1c} ≥0.08 Metformin dose <1,500 mg/day	Hb A_{1c} <0.08	Total
Study subjects, No.	233	105	434	772
Mean Hb A_{1c} level†	9.0‡	9.0‡	7.2§	8.0
Age, yr	61.2‡	62.2§	63.6§	62.7
Sex, female, No. (%)	86 (36.9)‡	49 (46.7)§	225 (51.8)‖	360 (46.6)
Race, white, No. (%)	217 (93.1)‡	95 (90.5)§	411 (94.7)‡	723 (93.7)
BMI	31.7	32.0	31.6	31.7
Years since diabetes mellitus recognized	9.7‡	9.1§	8.1§	8.7
1997 average daily metformin dose, mg	2,223‡	955§	1,864‖	1,849
Years taking drug	1.1‡	0.7§	1.1‡	1.0
1997 prescription fills of metformin	7.1‡	5.5§	7.3‡	7.0

Hb A_{1c} = glycosylated hemoglobin (hemoglobin A_{1c}); BMI = body mass index.
*Except as otherwise noted, data are mean values. Figures with different symbols (‡, §, and ‖) are significantly different from each other ($P<0.05$).
†Expressed as a proportion of 1. For conventional units, multiply by 100 to obtain percentage.

more prescription fills than those who were well controlled. By definition, these patients are in secondary sulfonylurea failure[11] and are candidates for the addition or substitution of insulin, metformin, rosiglitazone, or pioglitazone.

Second, of the 1,346 patients using insulin alone or in combination with sulfonylureas or metformin, 563 (41.8%) failed to achieve glycemic control below the recommended threshold. Most (n = 393 [29.2%]) were taking an average of 60 units of insulin daily, suggesting that they were not administering enough insulin to achieve adequate control. By comparison, insulin users with Hb A_{1c} values of less than 0.08 averaged 90 units per day.

Third, 170 insulin users (12.6%) who had an Hb A_{1c} of 0.08 or above were receiving high doses of insulin—averaging 164 units per day—reflecting the insulin-resistant character of type 2 diabetes mellitus. These patients may benefit from increases in their insulin dose. However, only 26 (15.3%) of these 170 relatively younger patients were supplementing their insulin with metformin. Adding newer oral agents such as metformin, rosiglitazone, or pioglitazone might improve their glycemic control.

Fourth, of those using metformin alone or in combination with sulfonylureas, nearly half (43.8% [n = 338]) had not achieved glycemic control (Hb A_{1c} level <0.08). Most of these metformin users (30.2% [n = 233]) received sufficient doses of their drug, averaging more than 2,200 mg per day. Failure to achieve good control at this level of metformin dosing suggests that insulin therapy should be started for these patients. Another 105 of those metformin users whose Hb A_{1c} values remained above the recommended glycemic goals (13.6%) received an average dose of less than 1,500 mg per day, which may reflect subtherapeutic dosing. These patients had been receiving metformin for a much shorter period (about 8 months) and received fewer prescription fills of metformin than all other metformin users, so some of this subtherapeutic dosing may reflect the initiation of therapy with low doses. On average, however, their mean duration of therapy (8.4 months) was sufficient to titrate to full therapeutic dosing.

A limitation of the current study was the exclusion of 13% of the potential study population because the subject did not have an Hb A_{1c} measurement (9%) or because the therapeutic regimen of the subject could not be assessed (4%). Whether these subjects differ from those included with respect to glycemic control or pharmacotherapy cannot be determined, but the "take-home messages" of the results presented here are not biased by the exclusion of these subjects.

In summary, a substantial number of persons (1,570 [31.0%]) with type 2 diabetes mellitus might improve their glycemic control with simple adjustments to their pharmacologic therapy. Of the 901 users of either insulin or metformin who had not achieved glycemic control, 498 (55.3%) might achieve better glycemic control merely by increasing their doses. Many patients manifesting secondary failure of sulfonylurea therapy, nevertheless, were continued on this therapy, rather than being switched to combination therapy or having insulin added to their regimen.

Busy clinicians with heavy workloads can enhance their management of diabetes by identifying patients whose glycemic control could be increased through a change in medication or simple adjustment in dosage. Even within clinician practices and health care organizations performing well by recommended standards, there may still be room for improvements—improvements that are affordable and within reach.

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COMMENTARY

The target for good glycemic control should be an Hb A_{1c} concentration of less than 0.07

Facts are stubborn things; and whatever may be our wishes, our inclinations or the dictates of our passions, they cannot alter the state of facts and evidence.

John Adams in defense of the British soldiers on trial for the Boston Massacre in 1770

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Nichols and colleagues' conclusion, that a substantial number of patients with type 2 diabetes might improve their glycemic control with simple adjustments of their pharmacologic therapy, is appealing but only half true. At this complex intersection of metabolic, psychological, environmental, and life-style disease, it is unlikely that a "simple" solution will do the trick. If it did, we all would have adopted it long ago.

The authors chose an Hb A_{1c} concentration of less than 0.08 (<8%) as the recommended standard of care, which is questionable. Their standard may stem from a misinterpretation of the Health Plan Employer Data and Information Set (HEDIS) measures, based on the original consensus of the Diabetes Quality Improvement Program.[1] This program used an Hb A_{1c} value of less than 0.08 as a measure of improvement in caring for patients with type 2 diabetes who started with much higher levels, but this was never intended as a target or a definition of "good control." The target for good control in type 2 diabetes should be an Hb A_{1c} of less than 0.07.[2] The UK Prospective Diabetes Study (UKPDS) showed that intensive glycemic control was substantially better than conventional treatment in reducing diabetes-related microvascular end points.[2] In this 10-year study, the average Hb A_{1c} level was 0.079 in the group receiving conventional treatment and 0.07 in the intensive treatment group.

The Kaiser Permanente patients, with a mean BMI of 31.1, were obese and significantly heavier than the UKPDS cohort, whose mean BMI was 27.5. Those diabetologists whom God wishes to destroy, He first makes treat type 2 diabetes with diet. This remains a cornerstone of therapy. Yet, Nichols and colleagues fail to emphasize this important, if frustrating, treatment modality.

Many of the conclusions are worthwhile take-home messages. Clinicians often continue sulfonylureas long after it is evident that they have failed, they delay dose escalation, they often fail to use combination therapy, and they delay the initiation of insulin. In this regard, we should note that most (75%) of the hypoglycemic effect of sulfonylureas is achieved at a daily dose approximating half of the maximally effective dose. Similarly, 80% to 85% of the maximal glucose-lowering effect of metformin is seen at a daily dose of 1,500 mg. Increasing the dose of these drugs is unlikely to provide additional benefits, and it often leads to more side effects.[3]

After all is said and done, reducing the Hb A_{1c} level—a surrogate end point—is currently where "the rubber meets the road." When all else fails, insulin, often in large doses, is necessary in these insulin-tolerant patients. Often, both

the patient and physician resist this logic far too long. Is this another kind of "insulin resistance"?

Finally, since the study occurred in 1997, there are no data regarding the use of currently available thiazolidinediones,[4] rosiglitazone and pioglitazone, nor of repaglinide.[5]

While walking by a lake, a physics professor saw a house on fire. He noted the fire and the lake filled with water close by. He knew that water put out fire, and having solved this intellectual problem to his satisfaction, he continued on his way. It's hard work applying such simple principles in the real world of diabetes.

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Participation in maternal serum screening for Down syndrome, neural tube defects, and trisomy 18 following screen-positive results in a previous pregnancy

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ABSTRACT **Objective** To determine whether women who have had a positive serum screening result for Down syndrome or neural tube defect in 1 pregnancy have a lower rate of participation in screening in their next pregnancy. **Setting** A triple-marker screening program at a university hospital. **Methods** Pregnancy and screening information was collected from laboratory and hospital databases to compare subsequent screening participation of women who were screen-negative and screen-positive for the risk of a fetus with Down syndrome or a neural tube defect. **Results** In an age-matched comparison, 108 women who had a previous screen-positive result were significantly less likely than 108 women who were screen-negative to participate in maternal serum screening in their next pregnancy. When examined according to the type of screen-positive result, the effect was significant for both those who were screen-positive for Down syndrome and those who were screen-positive for neural tube defect. The degree of risk in screen-positive women did not significantly affect their participation in screening in the next pregnancy. **Conclusions** Anxiety related to a screen-positive result probably causes decreased participation in maternal serum screening in the next pregnancy. Reducing the screen-positive rate in prenatal serum screening would alleviate maternal anxiety and would probably lead to more stable participation.

Maternal serum screening, performed at 15 to 20 weeks of pregnancy, is commonly used in the prenatal detection of open neural tube defects, Down syndrome, and trisomy 18. By its nature as a screening test, maternal serum screening cannot determine with certainty if the baby is affected with a fetal anomaly. Most women who receive screening results indicating a high risk (screen-positive) have unaffected babies (false-positive), and some receiving results indicating a low risk (screen-negative) have affected babies (false-negative). Risk cutoffs are chosen to optimize the detection rate while maintaining a relatively low (5%-10%) false-positive rate.

Farrant first reported that false-positive results were associated with higher levels of maternal anxiety.[1] All subsequent studies of women who received false-positive results, indicating an increased risk of Down syndrome or neural tube defects, have confirmed this observation.[2-9] Heightened anxiety was found to persist in screen-positive patients even after their initial positive results were shown to be false.[2,10] It is not surprising, then, that women with false-positive results, compared with those with true-negative results, were more opposed to maternal serum screening[11,12] and were less likely to say that they would choose maternal serum screening in a future pregnancy.[11,13] However, whether this negative attitude translates into reduced screening participation in a future pregnancy has not yet been reported.

The purpose of this study was to determine whether women who have had a positive serum screening result in 1 pregnancy have a lower rate of participation in screening

in their next pregnancy than women who were screen-negative in their previous pregnancy. We also examined whether it made a difference if women were screen-positive for Down syndrome or neural tube defect or whether the degree of increased risk made a difference in subsequent screening participation. Finally, we asked if screen-positive women who declined serum screening in their subsequent pregnancy chose other forms of prenatal testing instead, such as amniocentesis or ultrasound examination.

PATIENTS AND METHODS

All women who underwent maternal serum triple-marker screening at the Women and Infants Hospital, Brown University School of Medicine, Providence, RI, in 1994 and who had a subsequent pregnancy at Women and Infants Hospital before May 1998 were eligible for inclusion in this study. Women who were screen-positive for trisomy 18, for both Down syndrome and neural tube defect, who had a previous pregnancy with fetal neural tube defect or Down syndrome, and those who were carrying twins during their 1994 pregnancy were excluded.

Our study population was identified using the 1994 comprehensive laboratory screening log book. Of the 9,250 screenings performed in that year, 14% of women had initial screen-positive results—9% for Down syndrome, 4.5% for neural tube defect, and 0.5% for trisomy 18. The screening test result was considered positive if the second-trimester risk for Down syndrome was 1 or more in 270 pregnancies.[14] A screen-positive result for the risk of neural tube defect was defined as a maternal serum α-fetoprotein (AFP) level 2 or more multiples of the median (MoM).[15] A screen-positive result for risk of trisomy 18 was defined as a maternal serum AFP level of 0.75 or less (MoM), a human chorionic gonadotropin level of 0.55 or less (MoM), and an unconjugated estriol level of 0.60 or less (MoM).[16] Of the 1,295 women with positive screening results in 1994, 108 were identified as being screen-positive for either Down syndrome or neural tube defect and as having a second pregnancy before May 1998.

A screen-negative group was identified in a similar manner. Women who had negative results on screening tests performed in 1994 were reviewed in the hospital database. Women who were screen-negative in 1994 and who had a subsequent pregnancy between 1994 and May 1998 were selected as a control group, with each control matched with 1 screen-positive case for maternal age at second delivery (±1 year).

Serum screening information on the study population was obtained using a laboratory reporting system (Alpha; Logical Medical Systems, London). For women receiving screen-positive results, medical records and the laboratory database were examined to determine whether maternal serum screening or alternative prenatal testing (chorionic villus sampling, amniocentesis, or targeted ultrasonography performed between 16 and 24 weeks) was chosen in the subsequent pregnancy.

Table 1 *Participation in subsequent screening according to the result of the screening test in the previous pregnancy*

Result of screen in previous pregnancy	Total No.	No. (%) having screening in subsequent pregnancy	OR (95% CI)
Screen-negative	108	85 (79)	0.36 (0.20–0.66)
All screen-positive	108	62 (57)*	
DS screen-positive only	60	31 (52)†	0.42 (0.20–0.90)
NTD screen-positive only	48	31 (65)‡	0.26 (0.09–0.74)

OR = odds ratio; CI = confidence interval; DS = Down syndrome; NTD = neural tube defect.
*P = 0.001 relative to matched screen-negative.
†P = 0.02 relative to matched screen-negative.
‡P = 0.009 relative to matched screen-negative.

DATA ANALYSIS

To assess differences in screening participation in the subsequent pregnancy according to previous screening results and type of screen-positive result, χ^2 analysis was performed (StatView; Abacus Concepts, Inc, Berkeley, CA). The odds ratios and 95% confidence intervals of those having screening in a subsequent pregnancy for women having a positive screening test result in the previous pregnancy, compared with those having a negative screening test result, were also calculated. χ^2 Tests for trend with 1 *df* were used to compare the participation in maternal serum screening in the subsequent pregnancy according to the degree of risk increase for the previous screen-positive pregnancy. A significant difference was accepted at $P<0.05$.

RESULTS

The participation of women in screening in their subsequent pregnancy according to their previous screening results is shown in table 1. In the 108 previously screen-negative and -positive women matched by maternal age, a significantly smaller percentage of those who were screen-positive (57% vs 79%, $\chi^2 = 11.27$; $P = 0.001$) had screening in their subsequent pregnancy. Overall, the effect of a screen-positive result was to reduce the odds of a woman having serum screening in a subsequent pregnancy by 64%.

Of the 108 previously screen-positive women, 60 were screen-positive for risk of a child with Down syndrome, and 48 were screen-positive for risk of a child with neural tube defect. As shown in table 1, women who were screen-positive for risk of Down syndrome participated in subsequent maternal serum screening significantly less often

Table 2 *Participation in subsequent screening given a screen-positive result for either Down syndrome or neural tube defect in the previous pregnancy, stratified by degree of increased risk of previous result*

Down syndrome			Neural tube defect		
Degree of increased risk in previous pregnancy	Total No.	No. (%) having screening	Degree of AFP elevation in previous pregnancy, MoM	Total No.	No. (%) having screening
1/201 to 1/270	17	10 (59)	2.00–2.49	31	20 (65)
1/101 to 1/200	24	12 (50)	2.50–3.49	13	9 (69)
1/100 to >1/2	19	9 (47)	≥3.50	4	2 (50)

AFP = α-fetoprotein; MoM = multiple of the means.

than women who were screen-negative (52% vs 72%, $\chi^2 = 5.08$; $P = 0.02$). Women who were screen-positive for risk of neural tube defect also participated in subsequent screening less often than their matched screen-negative controls (65% vs 88%, $\chi^2 = 6.92$; $P = 0.009$). The effect of a Down syndrome or a neural tube defect screen-positive result was to reduce the odds that a woman would have screening in a subsequent pregnancy by 58% and 74%, respectively. This reduced participation was not dependent on the degree of increased risk for either Down syndrome ($P = 0.50$) or neural tube defect ($P = 0.79$; table 2).

Forty-six of the previously screen-positive women declined serum screening in their subsequent pregnancy. Of the 41 of these women for whom follow-up information could be obtained for their second pregnancy, 18 (44%) had no prenatal testing in the second trimester, 14 (34%) had a second-trimester ultrasound examination, 8 (20%) had amniocentesis, and 1 had chorionic villus sampling. All of the 9 women having amniocentesis and chorionic villus sampling were aged 35 or older.

DISCUSSION

The present study shows that women receiving screen-positive test results in 1 pregnancy are less likely than women receiving negative results to participate in screening in their subsequent pregnancy and that the degree of risk of a screen-positive woman does not appear to influence her decision about screening in her next pregnancy. These findings are not surprising, given that women receiving positive screening results experience anxiety[2-9] and exhibit negative feelings toward serum screening.[11,12] Both those who were screen-positive for having a child with Down syndrome and those who were screen-positive for having a child with neural tube defects were less likely than screen-negative women to have screening in the future.

Marteau has shown that anxiety associated with screen-positive results would be reduced if before they are tested women knew more about the purpose of screening, the possibility of receiving positive results, and the sequence of decisions and procedures that may follow.[17] Other studies have shown that some women who had screening would not have chosen to undergo testing if they had been given more information before being tested,[18,19] and conversely, some women who were not screened would have chosen to participate.[20] In practice, however, comprehensive and even accurate information about prenatal testing is not always provided by obstetricians and midwives,[21] perhaps because they do not fully understand maternal serum screening.[22] In addition, evidence shows that women are poorly informed about the screening tests[23] and the implications of test results.[24] Improved patient education may increase the likelihood that previously screen-positive women would participate in screening in future pregnancies. We can be assured, however, that many women who receive positive results and decline screening in their subsequent pregnancy are accepting other prenatal tests in later pregnancies.

Although improved patient education on prenatal screening and better understanding of the consequences of a screen-positive result are valuable, the fact remains that current screening for Down syndrome and neural tube defects is associated with many false-positive results. In triple-marker screening, for example, about 5% of all screened women are offered amniocentesis because of their risk of a Down syndrome pregnancy, and another 2% are offered either targeted ultrasonography or amniocentesis because of their risk of a neural tube defect. In women who are screen-positive for Down syndrome, by the triple-marker test, the odds of having an affected fetus are of the order of 1 in 60, meaning that for every true-positive result, there will be 60 false-positive results. As the years go by, the number of women with false-positive screening results will grow substantially, and based on our results, participation in screening will decline.

Now that detection rates for Down syndrome are approaching and may surpass 80%, through the use of second-trimester 4-marker testing and first-trimester combined serum specimen–ultrasonography testing, efforts should focus on reducing the false-positive rate. This

would decrease the number of women experiencing anxiety because of screen-positive results and would improve the safety of the diagnostic process by decreasing the number of women having to be offered amniocentesis. As an example of this approach, a recent study by Wald and colleagues in which markers measured in the first and second trimesters were integrated into 1 risk assessment showed that a detection rate of 85% can be attained at a false-positive rate of less than 1%.[25] With this approach, not only would the number of amniocentesis procedures be reduced by more than four fifths, but the odds of having an affected fetus if a woman is screen-positive would be increased to about 1 in 7. Having fewer screen-positive results may translate into more stable participation in the prenatal screening process.

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COMMENTARY

What can we do to prepare patients for test results during pregnancy?

Screening for Down syndrome, neural tube defects, and trisomy 18 with maternal serum AFP is considered by some to be a routine part of pregnancy care. The American College of Obstetrics and Gynecology and the United States Preventive Services Task Force recommend offering maternal serum AFP screening to all pregnant women between 16 and 18 weeks of their pregnancy.[1]

The interval between having a positive screening test result and finding a definitive answer is stressful. According to Rausch and colleagues, this anxiety was the cause of decreased participation in maternal serum screening in subsequent pregnancies. The study suggests that providers of maternity care do not do enough to prepare women for the possibility of a false-positive test result. Anxiety about abnormal test results is the opposite of what women desire from prenatal testing. Expectant women often tell me that they just want to know that their baby is normal. Patients are anxious after having a positive test result, and the anxiety often remains even after they learn that the result was falsely positive.

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It is interesting that maternal serum AFP testing has become a de facto standard of care without the evidence that would typically be required to support a screening test. A recent article by Rogers reminds us that a screening test should follow the principle of primum non nocere: "first do no harm."[2] Physicians should consider 3 elements before offering a screening test.[3]

The burden of suffering from a disease is the prevalence of the disease in combination with the morbidity or mortality associated with that disease. The burden associated with the genetic diseases that maternal serum AFP screening can detect is certainly high enough to justify screening. Neural tube defects, for example, occur in 3 to 4 per 10,000 live births—a relatively common genetic disorder.

The screening test must be effective. The test should minimize the number of false-positive test results while maximizing the true-positive results. The likelihood that a positive test result means that someone has the disease (known as the positive predictive value) should be high. The test should not be prohibitively expensive, and the side effects of the screening test should be minimal. One of the problems with maternal serum AFP testing is the high number of false-positive results. Most women who test positive will have a normal fetus. The consequences of a positive test result may include amniocentesis, ultrasonography, and increased fetal surveillance. Other harm from a positive screening test result can include labeling, anxiety, and the increased costs associated with the additional workup.

The third element of a screening test is the evidence that screening actually prevents morbidity or mortality. With prenatal screening, this is critical because finding some disorders earlier in pregnancy—for example, intrauterine growth retardation—can affect the management of the pregnancy. No trials have shown improved outcomes of patients who have undergone screening for Down syndrome or neural tube defects.

So, what should physicians do with obstetric patients? Rausch and associates have documented the effects of false-positive screening test results during pregnancy on patient anxiety. It is important to obtain informed consent before ordering maternal serum AFP screening. Patients should understand the risks of false-positive and -negative test results and should know the consequences of a positive result and subsequent testing options. After they have received all of the information, they can make an informed choice about whether or not to have the test. Physicians should also counsel patients adequately about their results. We have a responsibility to evaluate the evidence behind screening tests before we offer them and to prepare obstetric patients for the "harm" that they may cause.

Dr Delzell cochairs the Group on Family-Centered Perinatal Care for the Society of Teachers of Family Medicine.

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capsule

Walnuts and macadamia nuts benefit lipid profiles Like walnuts, macadamia nuts can improve serum lipid profiles (*Arch Intern Med* 2000;160:1154-1158). Although a macadamia nut is 75% fat, most of the fat is monounsaturated. In a crossover experiment, replacing the 37% fat in a typical US diet with fat from macadamia nuts had a statistically significant impact on serum lipid parameters.

capsule

Acupressure bands don't prevent nausea It would be wonderful if a simple acupressure wristband reduced nausea and vomiting after surgery, but it doesn't seem to (*Can J Anaesth* 2000;47:319-324). A large randomized trial comparing the real thing with a sham wristband after endoscopic urological procedures found no difference between groups. Other investigators have had more luck with acupuncture, but it's more invasive and therefore less convenient.

Journal Digest

In people with no evidence of cardiovascular disease, how effective are interventions aimed at controlling risk factors in reducing all-cause and coronary artery disease mortality?

Ebrahim S, Davey Smith G. Multiple risk factor interventions for primary prevention of coronary heart disease. *Cochrane Review*, latest version February 24, 1999. In: the Cochrane Library. Oxford: Update Software.

DATA SOURCES

Studies were identified by using MEDLINE (1966-April 1995) and bibliographies of relevant studies and by contacting experts.

STUDY SELECTION

Studies were selected if they were randomized controlled trials with 6 months or more of follow-up of counseling or educational interventions, with or without medications aimed at controlling 1 or more cardiovascular risk factors—blood pressure, smoking, total blood cholesterol level, physical activity, and diet—in people aged 40 years or older who show no evidence of cardiovascular disease.

DATA EXTRACTION

Data were extracted independently by 2 reviewers on study design aspects, patient baseline characteristics, and follow-up. Outcomes were changes in blood pressure and total blood cholesterol level, smoking, all-cause mortality, and coronary artery disease (CAD) mortality.

MAIN RESULTS

Eighteen trials (140,245 patients) were included. Heterogeneity existed among the trials for all outcomes except CAD mortality (2 trials focused on hypertensive patients). Blood pressure, total blood cholesterol level, and smoking prevalence decreased more in patients who received risk factor modification than in patients who received no intervention or usual care (table). Ten trials included clinical outcomes. All-cause and CAD mortality rates were not reduced by risk factor modification (table).

CONCLUSION

In people who show no evidence of established cardiovascular disease, multiple risk factor interventions consisting of either counseling or educational interventions modestly reduce blood pressure, total blood cholesterol level, and smoking prevalence but not all-cause or CAD mortality.

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*Risk factor intervention vs no intervention for coronary artery disease (CAD)**

Outcomes (follow-up range, 6 mo-12 yr)	Weighted mean decrease (95% CI)
Systolic blood pressure, mm Hg	3.3 (1.9-4.7)
Diastolic blood pressure, mm Hg	2.2 (1.3-3.1)
Total blood cholesterol level, mmol/L	0.16 (0.09-0.24)

	Weighted event rates			
	Intervention	No intervention	RRR (CI)	NNT (CI)
Smoking prevalence (follow-up range, 1-12 yr), %	34.5	38	10 (2-17)	Baseline prevalence, 40% = 25 Baseline prevalence, 15% = 67
All-cause mortality, %	7.1	7.2	5 (−4-13)	Not significant
CAD mortality, %	2.5	2.6	4 (−4-11)	Not significant

CI = confidence interval; RRR = relative risk reduction; NNT = number needed to treat.
*Random effects model used for all outcomes except CAD mortality.

COMMENTARY

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Ebrahim and Smith conclude that counseling or education to reduce cardiovascular risk factors fails to reduce all-cause mortality or mortality from CAD. This conclusion is not surprising because patients included in these studies were from the general population, at average risk for CAD, and the trials had a median follow-up of 3 years. The benefits of risk factor reduction may develop after many years.

All risk factors are not created equal. The potential benefits of behavioral approaches to reduce tobacco use in average-risk patients are greater than those of counseling to alter diet or increase exercise. The cost-effectiveness of smoking cessation programs is <$1,000 per life-year saved.[1] Also, the potential benefit of adjunctive pharmacologic therapy to counseling or education needs to be emphasized. The addition of a 9-week course of sustained-release bupropion hydrochloride, with or without nicotine replacement therapy, to a brief program of physician advice and counseling may produce 1 year abstinence rates of greater than 30%.[2]

Finally, not all patients are equally motivated to change their lifestyle. Intensive lifestyle changes in motivated patients with established disease can decrease the incidence of cardiac events.[3] The potential effect of lifestyle modification in motivated, high-risk patients may be substantial.

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Can the prophylactic use of raloxifene, a selective estrogen-receptor modulator, prevent bone mineral loss and fractures in women with diagnosed osteoporosis or vertebral fractures?

Ettinger B, Black DM, Mitlak BH, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. *JAMA* 1999;282:637-646.

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DESIGN

A 36-month randomized, blinded, placebo-controlled study.

SETTING

A multicentered trial in 25 countries; more than half the participants were from the United States and Canada.

PARTICIPANTS

A total of 7,705 women, aged 31 to 80 years, who were at least 2 years postmenopause and either had osteoporosis by criteria of the World Health Organization or 1 or 2 vertebral fractures diagnosed by radiography. Ninety-five percent of the women were white. The mean age of the total group was 67 years. Twenty-six to twenty-nine percent of women had previously received estrogen therapy, and this did not vary significantly between the placebo and treatment groups. About one fifth of the women had had hysterectomies. Osteoporosis was diagnosed by a bone mineral density (BMD) *t* score (which is the deviation from values for young adults) of −2.5 SDs. Women who had used estrogen, androgens, calcitonin, biphosphonates (all medications used to treat osteoporosis), steroids, or antiseizure drugs within 3 months were excluded. Women who had bone disease; endocrine disorders; renal or liver disease; alcoholism; endometrial, breast, or other cancer; undiagnosed uterine bleeding; a history of thrombotic events; or more than 2 vertebral fractures or pathologic fractures were also excluded.

INTERVENTION

Women were classified as group 1 (women diagnosed with osteoporosis) or group 2 (women with ≥1 moderate to severe or ≥2 mild to moderate vertebral fractures and reduced BMD). They were then randomly allocated to 1 of 3 groups. One group received raloxifene hydrochloride, 60 mg daily; the second received raloxifene, 120 mg daily; and the third received a placebo. All women were placed on a daily regimen of calcium, 500 mg, and vitamin D, 400 to 600 mg IU. The women were then observed for 36 months.

MAIN OUTCOME MEASURES

Development of vertebral fractures diagnosed by radiography, reported nonvertebral fractures, and spine and femoral neck BMD as measured by dual-energy x-ray absorptiometric scans.

MAIN RESULTS

The use of raloxifene at both doses significantly reduced the number of vertebral fractures over 36 months compared with placebo. Raloxifene use reduced vertebral fractures by 51% in women with osteoporosis (group 1) and by 30% (60-mg dose) and 50% (120-mg dose) in those with vertebral fracture (group 2). For every 100 women in treated in group 1, raloxifene prevented 2.3 vertebral fractures (relative risk [RR] = 0.5). For every 100 women in group 2, raloxifene at 60 mg daily prevented 7 vertebral fractures (RR = 0.7) and at 120 mg daily, it prevented 10.5 fractures (RR = 0.5).

Raloxifene did not significantly decrease the risk of nonvertebral fractures. When compared with women in placebo groups who had no change or a decrease in BMD, those who received raloxifene had a significant increase in BMD in the lumbar spine of more than 2%. Women who took raloxifene had an increased incidence of venous thrombosis (RR = 3.0). Breast cancer developed in 40 women. The women in the raloxifene treatment groups had a lower incidence of breast cancer. The women who took raloxifene had an RR of breast cancer developing of 0.2 to 0.6 compared with women who took placebo.

The risk of thrombosis was greater in the treatment group. The incidence of deep vein thrombophlebitis and pulmonary embolism combined was 0.3% in the placebo group, 1% of the group receiving the 60-mg dose of raloxifene, and 1% of the group receiving the 120-mg dose of raloxifene. The groups of women taking raloxifene had an RR of 3.1 for developing a thromboembolic event compared with the placebo group. For both groups taking raloxifene, for every 1,000 women, 7 additional thrombotic events occurred (RR=3.0). No deaths were reported in the study. Of all the women in the study, 24.7 % had serious side effects: 527 women of the raloxifene treatment group and 227 women in the placebo group withdrew from the study because of adverse effects ($P = 0.04$), including hot flashes, thromboembolic events, cancer, influenza syndrome, leg cramps, peripheral edema, hypertension, hypercholesterolemia, and hematuria.

COMMENTARY

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The secondary prevention of osteoporotic fractures and the reversal of osteoporotic BMD loss are important. Increasing BMD and reducing fractures may significantly reduce the cost of osteoporosis[1] through their effects on disability, loss of independence, nursing and nursing home placement, pain, and subsequent medical illness caused by vertebral fractures. The social and actual costs of osteoporosis to society are high.

Several large observational studies have shown that estrogen use is associated with a decreased incidence of osteoporosis and fractures.[2-6] In an international consensus development conference on osteoporosis, it was concluded that estrogen therapy is the only well-established preventive measure that could decrease the number of osteoporotic fractures.[7]

However, estrogen must be taken at least 7 years to produce this benefit. In the Heart and Estrogen/Progestin Replacement Study of 2,700 women with heart disease randomly assigned to receive estrogen and progestin or placebo for 4 years, there was no reduction in nonvertebral fractures with the use of estrogen-progestin.[8] Fewer than 15% of women in the United States take estrogen for more than 1 year.[9,10] The potentially fatal side effect of increased thrombotic events—especially in women who smoke, are obese, or have other physical disabilities restricting motion—the troublesome consequences of vaginal bleeding and other symptoms and fears of increased risks of cancer make the prophylactic use of estrogen, even in women with osteoporosis, difficult to justify. Calcium and vitamin D taken together daily have been shown to reduce the risk of fractures. Studies examining whether biphosphonates reduce the risk of vertebral and nonvertebral fractures are contradictory. The perfect agent for primary and secondary prevention of osteoporotic fractures has yet to be discovered.

Tamoxifen citrate, a selective estrogen-receptor modulator, has been successfully used in the treatment of breast cancer.[11] Studies are now examining the use of tamoxifen for the primary prevention of breast cancer in high-risk women. In studies of breast cancer treatment, tamoxifen, which has estrogen-antagonist effects in the breast and agonist effects in the bone and uterus, reduced the risk of fractures.[12] Tamoxifen has not been suggested for osteoporosis prophylaxis because of its association with endometrial cancer and thrombotic events with long-term use. Raloxifene use, with its antagonist effect on the uterus, does not increase the risk of endometrial cancer. It has been suggested as a prophylactic agent to prevent fractures in women who already have osteoporosis or osteopenia and vertebral fractures. Raloxifene also seems to prevent breast cancer and improve lipid profiles, although it produces a serious and increased risk of thrombotic events.

Two large studies that include raloxifene may provide additional clinical information. A trial of 22,000 postmenopausal women in the United States and Canada, known as the Study of Tamoxifen and Raloxifene

(STAR), will examine the use of these drugs on breast cancer incidence after 7 years. Secondary end points in the trial are osteoporosis, heart disease, and endometrial cancer. The Raloxifene Use for The Heart (RUTH) study will examine the drug's effects on cardiovascular disease.

The data from this study suggest that raloxifene therapy decreases the incidence of vertebral fractures and increases BMD, but some questions remain. Why was there no significant reduction in nonvertebral fractures in 3 years? Would longer use and follow-up show different or better results? Why did the improvement in BMD seem to plateau at 2 years? Is there any additional improvement with longer-term therapy, or are 2 or 3 years of treatment sufficient? An additional factor in this study is that it was supported completely by the maker of raloxifene (Eli Lilly & Company), and many of the authors have financial ties to this drug company.

Whether raloxifene will be a "miracle drug" for women, curing osteoporosis, decreasing heart disease, and preventing breast cancer, and whether its use is beneficial for all women need further study. Selective estrogen-receptor modulators may prove to be useful for conditions in which the use of estrogen-replacement therapies are precluded by their considerable side effects. Both tamoxifen and raloxifene are associated with a significantly increased risk of thrombosis. These 2 drugs, and their soon-to-be developed relatives, will need much closer evaluation before their use can be routinely justified. Closer long-term investigation is essential to see how these drugs will be important to all or some groups of women.

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A patient who changed my life
"You heard all wrong"

"If India's family planning policy has to succeed you all have a part to play."

As final year medical students, all unmarried, from conservative backgrounds, even the most macho men in my class were beginning to wish that our project was something different, perhaps a nice nutrition study.

The teacher handed out oblong, green packets decorated with a red triangle, the family planning symbol. "Go forth, convert the village, do your mite."

We assiduously covered the 40 families we had been assigned, month after month, checking the empty containers and making sure that schedules were being followed.

In the fourth house, the woman hissed into my ear, "I was due 4 days ago." I checked her packets and chart once more.

"Is the course completed?"

"Yes." She nodded her head vigorously.

"Each time?"

"Yes. I am nauseated, and I want to eat only lime pickle."

"Don't worry." I patted her back reassuringly.

Three months later, there was a distinct bulge in the lower part of her abdomen. I escorted her back to the base hospital and consulted the professor.

"Sir, we were told that the pill was 99.9% effective. Her pregnancy test is positive."

He pushed his spectacles up on to his bald head and turned to the patient, "Did you throw away the pills?"

"No, doctor."

"Did you take them regularly?"

"No."

I looked at her accusingly. "You told me you had not missed a single dose."

"No, doctor, you heard all wrong. I said that my husband did not miss a single dose."

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Migraine: pharmacotherapy in the emergency department

ABSTRACT **Migraine can be a disabling condition for the sufferer. For the small number of patients for whom home therapy fails and who seek treatment in an emergency department, several therapeutic options are available. I review the evidence regarding the effectiveness and safety of the following therapies: the phenothiazines, lignocaine (lidocaine), ketorolac, the ergot alkaloids, metoclopramide hydrochloride, the "triptans," haloperidol, pethidine (meperidine hydrochloride), and magnesium sulfate. Based on available evidence, the most effective agents seem to be prochlorperazine, chlorpromazine and sumatriptan, each of which has achieved greater than 70% efficacy in several studies.**

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Migraine headache can be a disabling condition. Patients and their general practitioners successfully manage most migraine headaches. However, a few fail to respond, and patients may present for treatment at emergency departments (EDs). Because most patients have tried oral medications before attending the ED, other routes of administration (usually parenteral) are most often used in ED. In this review, I focus on the agents that may be used to treat migraine in EDs and the evidence supporting their use.

DEFINITIONS

Most of the research in the area of migraine focuses on "common migraine" or migraine without aura. The Headache Classification Committee of the International Headache Society defines migraine without aura as an[1]

> idiopathic, recurring headache disorder manifesting in attacks lasting 4 to 72 hours. Typical characteristics are unilateral location; pulsating quality; moderate or severe intensity; aggravation by routine physical activity; and association with nausea, photophobia, and phonophobia.

The rarer migraine with aura is described as an[1]

> idiopathic, recurring headache disorder manifesting with attacks of neurological symptoms unequivocally localisable to the cerebral cortex or brain stem, usually developing gradually over 5 to 20 minutes and lasting less than 60 minutes. Headache, nausea and/or photophobia usually follow neurological aura symptoms directly or after a free interval of less than an hour. The headache usually lasts less than 72 hours, but may be completely absent.

At least 2 typical episodes are needed before this diagnosis can be assigned. In addition, there are a number of uncommon variants, such as ophthalmoplegic and abdominal migraine.

PATHOPHYSIOLOGY

The pathophysiologic features of migraine are complex, and our understanding continues to evolve. Events implicated in migraine initiation include altered electrical activity ("cortical spreading depression"[2]), a failure of brain ion homeostasis, an efflux of excitatory amino acids from nerve cells, and increased energy metabolism.[3] *N*-methyl-D-aspartate receptors are implicated in this process.[3]

The headache pain of migraine seems to result from the activation of the trigeminovascular system.[4-6] The triggers to the development of migraine headache are probably chemical and are thought to originate in the brain, blood vessel walls, and the blood. These triggers stimulate trigeminovascular axons, causing pain and the release of vasoactive neuropeptides from perivascular axons. These neuropeptides act on mast cells, endothelial cells, and platelets, resulting in increased extracellular levels of arachidonate metabolites, amines, peptides, and ions. These mediators and the resultant tissue injury lead to prolongation of pain and hyperalgesia.[6]

Serotonin has also been specifically implicated in migraine. By the activation of afferents, it causes a retrograde release of substance P. This in turn increases capillary permeability and edema.[7] In addition, magnesium has been suggested as having a role.[8]

The complexity of the mechanisms involved in the genesis of migraine makes it likely that to provide effective relief from migraine symptoms, the processes can be interrupted in several ways. Several pharmacologic agents and combinations of agents for the relief of migraine have been studied.

THERAPEUTICS

Most patients seen in EDs with severe migraine have tried to terminate their migraine headache with oral medication before going to the ED. Therefore, this review focuses on the agents that are appropriate for use in EDs. The important issues to be considered are their efficacy, the need for additional medication, and the incidence of "rebound" headache.

Problems with the evidence

An evidence-based review of the therapeutics of acute migraine is compromised by the quality of the evidence available. With the exception of the drug company–sponsored studies investigating the "triptans," most studies are small, with fewer than 50 patients in each subgroup being the norm. This means that the power of these studies to reach methodologically sound conclusions is limited. In addition, various measures of "success of treatment" are used by different study groups, which makes comparison difficult. Given these limitations, I attempt to pull together the available evidence to inform practice and form a basis for further research.

Phenothiazines: chlorpromazine and prochlorperazine

Phenothiazines are antipsychotic drugs. In the central nervous system, they are powerful antagonists of the neurotransmitter action of dopamine in the basal ganglia and limbic system. They are also potent antiemetics through effects on the chemoreceptor trigger zone, and neuroleptic actions seem to change pain perception. In addition, they are α-adrenergic antagonists (which can lead to orthostatic hypotension), chlorpromazine having greater α-blocking effect than prochlorperazine. And they have anticholinergic properties and are antagonists at both histamine and serotonin (5-hydroxytryptamine) receptors.[9]

Besides their hypotensive effect, the major side effect of phenothiazines in short-term use is dystonia. This is an idiosyncratic reaction and may occur after a single dose.[9] The mechanism by which phenothiazines act in migraine is uncertain. It is possibly the result of a combination of actions: antiserotonin effect, antidopamine effect in the chemoreceptor trigger zone, and vascular effects through their α-blocking action.[10]

The evidence about chlorpromazine

The table summarizes the success rates with the use of chlorpromazine.[11-15] Dosing regimens have varied, but a dose of 12.5 mg given intravenously (IV) and repeated at 20-minute intervals to a total dose of 37.5 mg would be representative. Intravenous fluids need to be given because of the substantial rate of orthostatic hypotension.

In comparative trials, chlorpromazine has been reported to be superior to meperidine hydrochloride (pethidine) (1 study),[16] lidocaine (lignocaine) (1 study),[14] and dihydroergotamine mesylate (DHE) (1 study)[14] and of similar effectiveness to ketorolac (1 study),[17] metoclopramide hydrochloride (1 study),[18] and sumatriptan (1 study).[15] None of the trials have reported any cases of dystonia resulting from the use of chlorpromazine in this way.

Success rates with the use of chlorpromazine to treat migraine

Study, year	Route administered	Patients, No.	Success rate, %
Lane and Ross,[11] 1985	IV	52	94
Iserson,[12] 1983	IM	100	96
McEwen et al,[13] 1987	IM	36	47
Bell et al,[14] 1990	IV	76*	89
Kelly et al,[15] 1997	IV	42	95

IV = intravenous; IM = intramuscular
*This study had 3 arms.

The evidence about prochlorperazine

Only a few small studies have been done of the use of prochlorperazine for migraine. Success rates of 67% to 92% have been reported.[19-22] Most studies use a dose of 10 mg IV.

In comparative studies, prochlorperazine has given better pain relief than sumatriptan (1 study),[22] metoclopramide (2 studies),[20,21] and ketorolac (1 study).[23] A preliminary report of the use of rectal prochlorperazine suppositories indicated good outcomes, but its design makes evaluation difficult.[24]

Ergot alkaloids

The pharmacologic activity of ergot alkaloids derives from their ability to interact to varying degrees with subtypes of adrenergic, dopaminergic, and tryptaminergic receptors.[9] Adverse effects of the ergot alkaloids related to their pharmacologic actions include peripheral vasoconstriction, peripheral gangrene, vomiting, nausea, chest pain, pruritus, and headache.[9]

The ergot alkaloids seem to exert their antimigraine effect by strongly binding to serotonin (subtypes 1B and 1D) receptors in the blood vessels of the dura and scalp, resulting in inhibition of the trigeminal nerve–mediated neurogenic inflammation.[6,25,26]

The evidence

Studies of DHE, either alone or in combination with metoclopramide or hydroxyzine, report success rates of 23%,[14] 73%,[27] and 93%[28] when used in the dose of 1 mg IV. In comparative studies, DHE has been more effective than meperidine (1 study)[28] or lidocaine (1 study),[14] less effective than chlorpromazine (1 study),[14] and of similar effectiveness to sumatriptan (1 study)[27] and meperidine (1 study).[29] Of particular note, in the only study in which adverse events were carefully collected, 55% of patients treated with DHE had severe gastrointestinal effects.[14]

Nasal sprays of DHE are also available. Headache relief

rates of 27% at 30 minutes and 70% at 4 hours have been reported.[30] One study suggests that DHE spray is less effective than sumatriptan given subcutaneously.[31]

Haloperidol

Haloperidol is a butyrophenone, heterocyclic antipsychotic agent. It has effects on the chemoreceptor trigger zone, reducing nausea and vomiting. It is an antagonist of the central effects of dopamine and is relatively selective for the dopamine-D_2 receptor. It is also a moderate α-antagonist peripherally and has antiserotonin effects. Haloperidol is less sedating than chlorpromazine and causes less orthostatic hypotension. Dystonic reactions are haloperidol's principal side effect.[9] It is postulated that haloperidol is effective in migraine because of its antidopamine or antiserotonin effects (or both).

The evidence

No controlled or comparative trials of the use of haloperidol in migraine have been published. In a case series of 6 patients with migraine treated with 5 mg of haloperidol IV after a bolus of 500 to 1,000 mL of IV fluids, complete or substantial relief was obtained in all patients within 25 to 65 minutes. Side effects were minimal.[32]

Ketorolac

Ketorolac is a nonsteroidal anti-inflammatory agent that inhibits prostaglandin synthesis, platelet aggregation, and serotonin release from platelets.[9] It is thought that nonsteroidal anti-inflammatory drugs may act in migraine by reducing the role of prostaglandins in increasing the sensitivity of blood vessel walls to pain and in regulating smooth muscle tone and reactivity as well as decreasing changes in vascular permeability.[33]

The evidence

The doses used in studies have been 30 to 60 mg intramuscularly (IM), and a success rate of 60% has been reported.[33] In comparative studies, ketorolac (at a dose of 60 mg) has been similar in effectiveness to meperidine (2 studies)[33,34] but at a dose of 30 mg IM was less effective than meperidine (1 study).[35] Ketorolac has been reported to be less effective than prochlorperazine (1 study).[23] A small study compared the use of ketorolac, 60 mg IM, with that of chlorpromazine, 25 mg IV, and found no difference in efficacy between the agents at 2 hours.[17] However, important methodologic problems make the value of this study questionable.

Lidocaine

Lidocaine is a class 1b antiarrhythmic agent (membrane stabilizer) used for the treatment of ventricular arrhythmia. It is also a potent local anesthetic agent.[9] It was hypothesized that lidocaine might act in migraine by its membrane-stabilizing effect, which inhibits the release of vasoactive substances from platelets, thus inhibiting the sterile inflammatory response.[14]

The evidence

The usual dose used in reported studies is about 100 mg. A randomized double-blind trial comparing IV lidocaine (1 mg/kg) with placebo failed to demonstrate a difference between the 2 for the relief of the head pain of migraine.[36] In comparative studies, lidocaine has been less effective than chlorpromazine (1 study)[14] and DHE (1 study).[14] A trial of nasal lidocaine spray at a concentration of 4% reported a success rate of 55%, but the early relapse rate was 42%.[37]

Metoclopramide hydrochloride

Metoclopramide is a nonphenothiazine central dopamine antagonist and a peripheral muscarinic agonist. It increases gastric emptying and is antiemetic at the chemoreceptor trigger zone.[9] It is postulated that metoclopramide acts in patients with migraine by its antiemetic effects combined with central antidopamine effects.[38] Side effects of metoclopramide use include drowsiness and dystonia.[9]

The evidence

Uncontrolled studies of metoclopramide have reported successful relief of migraine of 75%.[39] In a placebo-controlled trial, metoclopramide in a dose of 10 mg orally was found not to be superior to placebo in the relief of headache pain from migraine.[40] However, studies of IV metoclopramide report benefit over placebo[38,41] and, in 1, a success rate of 67%.[38]

In comparative studies, metoclopramide in a dose of 10 mg IM or IV has been less effective than prochlorperazine (2 studies).[20,21] High-dose metoclopramide (0.1 mg/kg dose IV for a total of 3 doses; average dose, 16 mg) was of similar effectiveness to chlorpromazine (1 study).[18]

Meperidine

Meperidine is a synthetic narcotic analgesic that exerts its pharmacologic activity principally by binding to opioid receptors. The main adverse effects of meperidine are nausea and vomiting, respiratory depression, drowsiness, and smooth muscle spasm, particularly in the biliary tree.[9] A major concern with the use of meperidine is the possibility of the development of dependence.[9] This concern is supported by the findings of a study of 1,900 patients with chronic headache, 5% of whom were narcotic abusers.[42]

It has been hypothesized that opioids are incapable of providing lasting, effective analgesia in migraine because they depend for their effect on serotonergic projections, and patients with migraine have been shown to have central nervous system serotonin depletion.[43]

The evidence

The usual dose of meperidine is 75 mg IM or IV. A literature search covering the years 1976 through 1999 failed to identify any placebo-controlled studies of the effectiveness of meperidine for the relief of migraine headache. Clinical success rates of 22% and 50% have been reported.[16,28]

In comparative trials, meperidine, either alone or in combination with hydroxyzine and dimenhydramine, has been less effective than DHE (1 study)[28] and chlorpromazine (1 study)[16] and of similar effectiveness to DHE (1 study).[29] With respect to ketorolac, meperidine was found to give better migraine relief than ketorolac in a dose of 30 mg IM (1 study),[35] but when the ketorolac dose was 60 mg IM, the agents had similar effectiveness (2 studies).[33,34]

Sumatriptan and other "triptans"

Sumatriptan is a specific and selective serotonin$_{1D}$ agonist that has no effect on other serotonin-receptor subtypes. This receptor is found predominantly in cranial blood vessels and constricts large blood vessels that may be dilated during episodes of migraine.[44] Sumatriptan may be administered orally, subcutaneously, or by nasal spray. Adverse effects include drowsiness, weakness, dizziness, flushing, rash, pruritus, increased blood pressure, chest pain, or chest tightness. Its use is contraindicated in patients with a history of ischemic heart disease, uncontrolled hypertension, or the concomitant use of ergot preparations. A substantial number of patients have no response, for which no clinical, pharmacokinetic, or genetic explanation has been found.[45]

The antimigraine effect of sumatriptan is thought to be attributable to its effect on the serotonin$_{1D}$ receptors in cranial blood vessels.[25,44] Sumatriptan and ergot alkaloids block neurogenic inflammation by acting at prejunctional serotonin receptors on trigeminovascular fibers.[6]

The evidence

Three large double-blind studies have compared the efficacy of sumatriptan in doses of either 6 mg or 8 mg subcutaneously with placebo. Clinical success rates were 70%,[46] 75% to 80%,[47] and 70%,[48] respectively. In each study, about half the sumatriptan-treated group reported mild adverse effects, including injection site reactions, nausea, flushing, and chest heaviness. Of patients successfully treated with sumatriptan, 34% to 60% reported recurrent headache within 24 hours.[47]

In comparative studies, sumatriptan when compared with DHE IV had a significantly higher rate of relief of headache at 2 hours, but there was no difference in the rate of relief at 3 to 4 hours.[27] Sumatriptan has been more effective than DHE nasal spray.[31] It has also been of similar effectiveness to chlorpromazine (1 study)[15] and less effective than prochlorperazine (1 study).[22] Sumatriptan-treated patients had a significantly higher rate of headache recurrence within 24 hours.

Newer triptans, such as rizatriptan benzoate (10 mg orally), have had success rates of about 75% to 80%.[49]

Sumatriptan is also now available as a nasal spray (20 mg), which has a reported clinical success rate of 63% to 78%.[50,51]

Magnesium sulfate

In migraine patients, magnesium sulfate has played an important part as a regulator of neuronal excitability and, hypothetically, of headache.[52] Magnesium concentrations may also have effects on serotonin receptors, *N*-methyl-D-aspartate receptors, and nitric oxide synthesis and release.[53] Evidence suggests that about 50% of migraine sufferers have reduced concentrations of ionized magnesium.[53]

The evidence

A preliminary study reports clinical success in 35 of 40 patients after infusion of 1 g of magnesium sulfate.[8] Response was more likely in those with low ionized magnesium concentrations.

SUMMARY

Review of the evidence has some clear implications for the management of migraine in EDs. Lidocaine fails to reach acceptable efficacy standards and, as such, is not recommended for use in acute migraine. Haloperidol and magnesium sulfate need to be studied in appropriate trials before conclusions can be drawn. Ketorolac, metoclopramide, and meperidine perform a little better, but each has been shown to be inferior to other treatments. The potential for dependence and abuse must also be considered with the use of meperidine. The data on DHE are difficult to interpret because it is often used in combination with other agents, for example, metoclopramide. However, it also has been less effective than chlorpromazine and sumatriptan in the treatment of acute pain and has a high rate of adverse effects. At this time, the most effective agents seem to be prochlorperazine, chlorpromazine, and sumatriptan, each of which in a number of studies has achieved greater then 70% efficacy.

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Best Practice

EVIDENCE-BASED CASE REVIEW

Diagnosis and treatment of deep vein thrombosis

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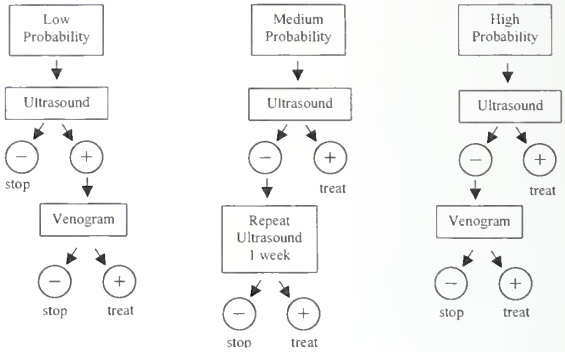
Ms Aviles, a 61-year-old moderately obese Ecuadoran woman with diabetes mellitus, osteoarthritis, and hypertension, saw her physician because for 3 days she had had pain and swelling in her left calf. She did not recall any trauma. On examination, her left calf diameter (measured 10 cm below the tibial tuberosity) was 3 cm larger than her right and was slightly tender to touch. She had bilateral varicose veins. The patient works as a housecleaner.



Diagnostic algorithm for evaluation of proximal deep venous thrombosis using ultrasonography and venography based on pretest probability.

METHODS

Searching the literature

For an introductory overview of the field, I searched OVID using the term "venous thrombosis." I limited the search to the subheadings "diagnosis," "local holdings," and "full text." Sixteen articles were found, of which 4 were recent review articles on deep venous thrombosis (DVT) in peer-reviewed journals.

Once I had formulated specific clinical questions, I searched OVID with the terms "venous thrombosis and thrombophilia" and "venous thrombosis/diagnosis and D-dimers." I chose studies that compared D-dimers with the venography, or less commonly, with an accepted diagnostic algorithm using ultrasonography.

Appraising the literature

I excluded studies that were not blinded and those that did not have explicit diagnostic criteria for deep venous thrombosis.

WHAT IS THE SIMPLEST AND MOST ACCURATE WAY TO DIAGNOSE DVT?

Clinical diagnosis is notoriously inaccurate for diagnosing DVT, although rules for making clinical predictions can be helpful. Table 1 demonstrates such a rule, developed by Wells and associates, that allows a determination of pretest probability.[1]

Based on the venography as a diagnostic standard—although magnetic resonance angiography has the potential to rival venography for accuracy—Doppler ultrasonography has a sensitivity and specificity of 95% for proximal DVTs (table 2). The ability to fully compress the popliteal and femoral veins with the ultrasound probe strongly excludes the diagnosis of DVT, and the lack of full compressibility strongly confirms the diagnosis. Doppler ultrasonography is more accurate for detecting symptomatic, proximal, and first-time DVTs than for detecting those that are asymptomatic, distal, or recurrent.[2]

Impedance plethysmography is less sensitive than Doppler ultrasonography.[3] D-Dimer assays have been developed to help rule out DVT. They have high sensitivity and negative predictive value but poor specificity.[4] A bed-

Table 1 *Clinical model for predicting pretest probability for DVT*

Clinical feature	Score*
Active cancer within 6 mo	1
Paralysis, paresis, or cast of lower extremity	1
Recently bedridden >3 d or major surgery within 4 wk	1
Localized tenderness along distribution of deep vein system	1
Calf diameter >3 cm larger than opposite leg†	1
Pitting edema	1
Collateral superficial veins (nonvaricose)	1
Alternative diagnosis as likely or greater than that of DVT	−2

*Interpretation: 0 = low probability = 3% frequency of DVT; 1-2 = medium probability = 17% frequency of DVT; ≥3 = high probability = 75% frequency of DVT.
†Measured 10 cm below tibial tuberosity.

side version of this assay may turn out to be the simplest and fastest way to rule out DVT, but a positive result would require confirmation because many other conditions such as malignant neoplasms, disseminated intravascular coagulation, and hepatic failure may cause elevated D-dimer levels. There is still no consensus on the appropriate cutoff value for a negative D-dimer result, but it may lie between 500 and 750 ng per mL.[5,6] The lower the cutoff point, the more reliably a DVT can be ruled out with a negative D-dimer result, but at the cost of additional false-positive results.

The diagnostic approach to DVT evaluation can differ based on pretest probability,[7] as determined by clinical characteristics outlined earlier (table 1).[8] For a patient with a low pretest probability, a normal-appearing Doppler ultrasonogram would be sufficient to rule out a DVT, and the patient could be reassured. Abnormalities seen on ultrasonography (a positive result) would require venography for confirmation. Conversely, in a patient with a high pretest probability, a positive finding on ultrasonography would be sufficient to begin treatment and a normal ultrasonogram would require venography for confirmation.

For a patient with moderate probability, a positive result on Doppler ultrasonography would permit the initiation of treatment, but a negative result would require a follow-up ultrasonogram in 1 week. If the second ultrasonography was again normal, the patient could be reassured, but a "newly" positive result on ultrasonography would be an indication for treatment. If the initial ultrasonogram was normal, there is evidence to suggest that a negative D-dimer test result at that time might obviate the need to repeat the ultrasonography at 1 week.[9]

Ms Aviles' physician had a moderate clinical suspicion for DVT, and a Doppler ultrasonogram obtained that afternoon revealed a distal DVT. The patient wanted to know if she had to take a "blood thinner" for the blood clot in her leg.

DOES EVERY PATIENT WITH DVT REQUIRE ANTICOAGULATION?

The main purpose of treating DVT is to prevent pulmonary embolism. Proximal DVTs (popliteal and higher) are associated with as high as a 50% incidence of pulmonary embolism if untreated[10]; therefore, anticoagulation should be instituted promptly. Distal DVTs propagate less than 20% of the time and usually do so within 1 week. Therefore, distal DVTs can be observed with serial ultrasonography (a second ultrasonogram 1 week later is usually sufficient), with treatment instituted only if proximal propagation is noted. The DVTs that remain confined to the calf are associated with a less than 1% risk of pulmonary embolism and a 2% chance of recurrent DVT.[11] If the results of the first ultrasonography are equivocal, however, or if they are normal in the face of a high clinical suspicion, venography should be performed.

Table 2 *Operating characteristics of diagnostic tests for proximal DVT**

Diagnostic test	Sensitivity, %	Specificity, %	Positive LR	Negative LR
Venography	~100	~100	Infinity	0
Doppler ultrasonography	95	95	19	0.05
Duplex ultrasonography	95	95	19	0.05
Impedence plethysmography	80	95	16	0.21
Iodine 125 fibrinogen scan	79	62	2.1	0.34
D-Dimer level	88-100	55-80	1.9-5.0	0.4-0.02

LR = likelihood ratio.
*From Black et al.[8]

If it turned out that Ms Aviles had a proximal DVT, would she have to be admitted to the hospital, or could she be treated as an outpatient?

All patients with proximal DVT require some form of heparin therapy until the dose of sodium warfarin is therapeutic. This has traditionally been with intravenous unfractionated heparin, and this is still the standard of care. The use of low-molecular-weight (LMW) heparin, however, may allow certain patients to avoid hospitalization.

The LMW form of heparin is depolymerized from unfractionated heparin and has a more predictable anticoagulant effect, thus avoiding the need to assess prothrombin times. It also promotes less antibody formation and is associated with a lower risk of heparin-associated thrombocytopenia. Hemorrhagic side effects appear to be similar to those with standard heparin. At least 2 studies have shown that patients treated at home with LMW heparin plus warfarin compare favorably with those treated in the hospital with intravenous heparin plus warfarin. The incidence of the recurrence of thromboembolism was 6.9% versus 8.6% in 1 study[12] and 5.3% versus 6.7% in the other.[13] The incidence of major bleeding was similar (0.5% vs 2%, and 2% vs 1%). A recent Cochrane Library review concluded that LMW heparin was at least as effective as unfractionated heparin and that its use was associated with a lower incidence of major hemorrhage and decreased overall mortality.[14]

Candidates for home therapy must be able to learn to

self-administer subcutaneously and to understand when to call their physician for adverse events. Alternatively, arrangements can be made for daily nurse visits. The medical facility must have a system in place for nursing oversight, troubleshooting, and organized follow-up. In these situations, outpatient treatment of DVT is feasible, equally efficacious, and probably cost-effective.[15,16] In many cases, these requirements will be difficult to meet, and the patient will require admission to the hospital for either intravenous or LMW heparin. In all of these patients, warfarin therapy should be initiated on day 1. The heparin (intravenous or LMW) can be discontinued after at least 4 to 5 days and when the international normalized ratio is greater than 2.0 for 2 consecutive days.

HOW LONG SHOULD ANTICOAGULATION LAST?

Two recent studies have led clinicians away from short courses of anticoagulation. In an open-label randomized trial, Schulman and colleagues compared 6 weeks with 6 months of warfarin therapy after a first DVT or pulmonary embolus.[17] Thromboembolic events recurred in 18.1% of the group receiving therapy for 6 weeks compared with 9.5% in the group treated for 6 months (absolute risk reduction [ARR] = 8.6%; number needed to treat [NNT] = 12). Kearon and associates conducted a randomized, double-blind trial of placebo versus warfarin after all participants had completed an initial 3-month course of anticoagulation.[18] The trial was halted at the 10-month interim analysis point because of a recurrence rate of 20.5% in the placebo group versus 1.3% in the group receiving extended warfarin (ARR = 19.2%, NNT = 5). Thus, for idiopathic first-episode DVT, anticoagulation should continue for at least 6 months. The optimal duration is unknown, although many clinicians cease treatment after 6 months.

The American College of Chest Physicians in the Fifth ACCP Consensus Conference on Antithrombotic Therapy admits that there is little solid evidence on which to base their duration guidelines for DVT in most clinical situations (table 3),[11] but they emphasize that age and prior thromboembolic events are powerful risk factors for recurrence.

Table 3 *Duration of anticoagulation for DVT**

Episode of DVT	Cause	Duration
First	Reversible or time-limited risk factors—surgery, trauma, short-term immobility, estrogen replacement	3-6 mo
First	Heterozygous factor V Leiden	3-6 mo
First	Idiopathic	At least 6 mo
First	Malignancy (until resolved), *homozygous* factor V Leiden, antiphospholipid antibody (until resolved), deficiency of antithrombin III, protein C or S	12 mo to lifetime
Recurrence		Probably lifetime

*Adapted from American College of Chest Physicians[11]

The physician sent Ms Aviles home with instructions to elevate the leg and take aspirin for pain. One week later, a second ultrasonogram showed no proximal extension of the clot. The physician prescribed support stockings for the varicose veins. She reassured Ms Aviles that the blood clot was unlikely to do serious harm, but she was unsure if she had to pursue an aggressive workup for thrombophilia or malignant neoplasm in this patient.

WHEN IS A THROMBOPHILIA WORKUP WARRANTED?

Numerous studies have analyzed the frequencies of genetic thrombophilias, but they have differed in their study populations and, therefore, have reported widely discordant hazard ratios. Activated protein C resistance and prothrombin gene mutations appear to be the most common of these thrombophilias. Deficiencies of protein S, C, and antithrombin III and the presence of antiphospholipid antibodies are less common. Homozygosity for the factor V Leiden mutation appears to confer a greater risk than heterozygosity. At least 1 study found no increased risk of recurrent DVT in subjects who were heterozygous for factor V Leiden without any other coexisting genetic defects.[19]

Although the ACCP suggests a slightly longer anticoagulation period for patients with protein C, S, and antithrombin III deficiencies and patients homozygous for the factor V Leiden mutation, little data support this. The argument could be made that knowledge of these thrombophilias would not change management substantially. It is true that these thrombophilias are likely associated with an increased incidence of recurrence, but any patient with DVT is at risk for recurrence, and advice about surgery, pregnancy, oral contraceptives, and the like should be the same. Also, as much as 10% of the general population may possess 1 or more of these inherited thrombophilias,

so the clinical significance may be difficult to interpret.

A reasonable approach might be to institute a thrombophilia workup for younger patients (possibly <50 years) who have an episode of DVT in the absence of any risk factors, those with a family history of thromboembolic disease, or patients with a thrombosis of unusual location or severity and to prolong anticoagulation accordingly. This will miss a certain number of people whose DVT was precipitated by a known risk factor but who also have genetic thrombophilias.

WHEN IS A WORKUP FOR MALIGNANT NEOPLASMS WARRANTED?

The yield of extensive evaluation for malignant lesions is low. In a population cohort in Denmark, it was found that 88 patients would have to be screened to uncover 1 excess cancer within the first year after DVT or pulmonary embolism.[20] Of cancers detected, 40% would already have metastasized. The strongest associations were with cancer of the pancreas, ovary, liver, and brain and in the first year only after the initial thromboembolic event. Another study that retrospectively analyzed patients younger than 40 years with DVT found no malignant neoplasms after a mean follow-up of 5 years.[21]

Beyond a thorough history and physical examination and age-appropriate cancer screening, there appears to be little utility in aggressive cancer workup after a first episode of DVT. Other secondary causes of DVT—nephrotic syndrome, congestive heart failure, myeloproliferative disorders—can usually be uncovered with the history, physical examination, and basic laboratory tests.

There was nothing in Ms Aviles' medical history to suggest cancer. There was no family history of clotting disorders. The physician performed a full physical examination, including breast and pelvic examinations, and ordered a mammogram and flexible sigmoidoscopy as part of regular screening. She told Ms Aviles that having 1 episode of DVT—even without knowing the cause—put her at risk for future DVTs and that she should be alert for situations that might provoke DVTs, such as immobilization, surgery, or estrogen therapy. She did not do a thrombophilia workup.

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TOPIC IN REVIEW

Reframing the professional ethic: the Council of Medical Specialty Societies consensus statement on the ethic of medicine

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INTRODUCTION

"Ethics makes us more critical of what we are doing—to bring us back daily to thinking about what it is to be a good doctor."[1(p38)]

Physicians are finding it difficult to apply ethical principles in an environment in which the views of their responsibilities are constantly shifting. Clinical decision making, the core of medical work, is influenced by competing interests, including those that are sometimes critical to physicians' livelihood. Does some common purpose remain in medical work that provides direction toward balancing these interests and clarifying physicians' responsibilities?

Traditional medical ethics, as embodied in the American Medical Association's *Code of Medical Ethics* (hereafter, the AMA Code of Ethics), has served as an ethical guide since the mid-1840s and has focused on physicians' responsibility to individual patients.[2] But the code fails to address other physician obligations adequately, such as providing universal access to health care and preventive services. Many observers, therefore, have called for a new ethic.[3-6]

CONSENSUS STATEMENT OF THE COUNCIL OF MEDICAL SPECIALTY SOCIETIES

The Council of Medical Specialty Societies (CMSS), an organization of national medical specialty societies, in 1995 established a task force on the ethic of medicine, culminating in a consensus statement in 1997 that was formulated by practicing physicians.

The consensus statement's 11 principles are prefaced by a preamble and framed in terms of physicians' relationships. Explanatory comments integral to each principle are contained in the complete statement (available at www.cmss.org). Rather than being a definitive document or supplanting any specialty society's code, the hope is that this statement of principles will provoke further discussion about, and the development of, an ethical foundation of medical care in an increasingly complex environment.

CMSS CONSENSUS STATEMENT ON THE ETHIC OF MEDICINE

Physician-patient relationship

1 The physician's primary inviolate role is as an active advocate for each patient's care and well-being.

2 The physician should treat each patient with honesty, compassion, dignity, and respect for individual autonomy.

3 The physician's commitment to patients includes health education and continuity of care.

Physician-physician relationship

4 Physicians have a responsibility to maintain moral integrity, intellectual honesty, and clinical competence.

5 Physicians, as stewards of medical knowledge, have an obligation to educate and share information with colleagues, including physicians in training.

RELATIONSHIP OF THE PHYSICIAN TO SYSTEMS OF CARE

6 The physician's duty of patient advocacy should not be altered by the system of health care delivery in which the physician practices.

Summary points

- Ethical principles are difficult to apply in today's constantly changing environment of health care
- An ethic of medicine must seek to balance physicians' obligation to individual patients with the professional, collective obligation to all who need medical care
- Physicians in both clinical and nonclinical work should remain focused on patients
- Terminally ill patients present complexities in care that require special ethical considerations
- We present a framework for ethical reflection that was developed by and for practitioners

Preamble

The practice of medicine is rooted in a covenant of trust among patients, physicians, and society. The ethic of medicine must seek to balance the physician's responsibility to each patient and the professional, collective obligation to all who need medical care. This statement articulates core values and principles that are shared by all physicians, in a range of settings and circumstances, including the use of new technologies of communication, regardless of specialty.

7 Physicians should resolve conflicts of interest in a way that gives primacy to the patient's interests.

8 Physicians should provide knowledgeable input into organizational decisions on the allocation of medical resources and the process of health care delivery.

Relationship of physician to society

9 Physicians have an obligation to serve the health care needs of all members of society.

10 Physicians have an ethical obligation to participate in the formation of health care policy.

11 Physicians have an ethical obligation to preserve and protect the trust bestowed on them by society.

Some of the values and principles that impinge on the relationship of physicians to their patients, colleagues, organizations, and the larger society in which they practice are introduced in this document. Further specifications can be developed to fit the particular needs of individual specialties, patient groups, and practice circumstances.

HOW CAN PHYSICIANS SERVE INDIVIDUAL PATIENTS AND SOCIETY?

A palpable tension permeates the consensus statement. Dr Edmund Pellegrino, the well-known medical ethicist, notes that physicians' obligations to both individual patients and to society are currently in conflict. Until this is resolved, physicians must remain focused on the patient, the foundation of the profession's ethical obligations, and cannot function as a double agent.[1,7]

Brody, however, argues that this patient-centered ideal is a "comforting myth," but one too far removed from reality to serve as a moral guide in times of such complex challenges to medical professionalism.[8] Hall and Berenson suggest as more realistic a group-based ethic that would encourage physicians to do the best they can with the resources available for their own patients and for others within the same practice group or insurance plan.[5] In addition, Bloche, a physician, lawyer, and ethicist, observes that physicians often work not directly with patients but within the justice system, insurance industry, and other social institutions. This paradigm of practice suggests that work for third parties creates no physician-patient relationship and, therefore, no primary obligation to the patient. This would appear to exempt physicians who ostensibly serve some societal goal from traditional ethical obligations.[2,9,10] Physicians who perform preauthorization reviews, for example, might not be held to the same ethic as those working directly with patients. Some states, however, have passed legislation that holds physicians serving as "medical directors" to the same obligations as treating physicians.

The authors of the CMSS statement maintain the primacy of physicians' duties toward patients even when they function outside of direct patient care (AMA Code of Ethics: opinion 8.02).[2] The final sentence in the preamble flows from this ideal: that all physicians as a group share core values and principles irrespective of their specialty, work setting, or circumstances of practice.

Case history

Dr Manville, a 55-year-old oncologist, is treating a terminally ill cancer patient with routine pain medication. A new medication that costs twice as much comes on the market and is advertised as providing better pain management. If Dr Manville chooses to prescribe the newer medication, his compensation from both his practice group and the managed care company that insures his patient will be affected. Is he obligated to disclose these financial arrangements to the patient? Dr Manville, in his best informed medical judgment, believes that the newer medication is not significantly better and decides against prescribing it. What if the patient demands the more expensive medication? What if the patient asks Dr Manville for an amount of the routine medication that could result in death if taken in overdose? If Dr Manville refuses, and the patient asks to be referred to a physician who might prescribe that amount of medication, what should Dr Manville do?

DISCUSSION OF CASE

Three consensus statement principles apply to this case:

Principle 7

A comment to principle 7 states "conflicts of interest are inevitable in medical practice. Physicians should disclose conflicts of interest to their patients, inform them of the impact of these conflicts on their medical care and of the options for their resolution."

If Dr Manville determines that the difference in efficacy between the current and new medication is insignificant, and he chooses not to prescribe the new one, financial disclosure is unnecessary. However, if his personal financial interest was a contributing factor in his decision, he would have to declare this to his patient.

If the data show that the new medication is more effective than the current one, Dr Manville is ethically obligated to consider prescribing it. Dr Manville must assess carefully the financial motivations in whatever decision he makes, and he must disclose these to the patient. As his patient's advocate, he should seek to include the medication in the formulary. Failing this, he should inform the patient of the drug's efficacy, its cost, and his financial conflict. Failure to prescribe the better medication because of income considerations or the hassle in-

Paul Mason/Photonica

Doctors have a duty to prescribe the most effective drug, even if it costs more

volved is ethically unacceptable. If the patient is unable to pay out-of-pocket expenses, Dr Manville may opt to prescribe it, accept the financial loss, and continue to lobby for its inclusion in the formulary.

Consensus statement authors support the current AMA opinion that obligates physicians to disclose both treatment options and financial incentives.[11] Some authors suggest that physicians are ill-equipped to explain their financial arrangements to patients and, in disclosing them, may undermine rather than enhance trust. These authors would place the obligation of the disclosure of financial concerns on the managed care plans rather than on physicians.[12]

Does joining a health maintenance organization, therefore, constitute a tacit agreement by the patient that there will be some limitations on the provision of medical care? Bloche suggests that disclosure either by the plan or by the physician does not dispense with the primary obligation of fidelity to the patient.[9]

Principle 8

A comment to principle 8 states that "physicians should advocate for the adoption of organizational policies that facilitate access to basic medical care." Dr Manville, therefore, is obligated to advocate for additions to the formulary if his patient will benefit materially. The AMA opinions on managed care and on prescription policies (AMA Code of Ethics: opinions 8.135 and 8.13) provide useful guidelines for physicians and managed care organizations.[2] Managed care companies should allow for sufficiently broad prescription guidelines and for the inclusion of new effective drugs. Physicians should read their contracts carefully regarding pharmaceutic use and appeal mechanisms. If a contract fails to provide a mechanism for implementing medical advances, for example, the plan may force physicians to practice below minimum standards and ethically require them to resign (AMA Code of Ethics: opinion 8.13-2G).[2]

Principle 2

In this case, after Dr Manville informed the patient that the difference in the drugs was insignificant, the patient remained adamant about trying the new medication. A comment to principle 2 states that "the physician should remain compassionate and dedicated to patients at the end of life, advise them and their surrogates of available options to alleviate pain and suffering, and use life-sustaining therapy appropriately." This comment does not imply that physicians necessarily should suffer financially in working to achieve these goals, but does alert them to the special needs of dying patients. Given recent advances in pain control, physicians are ethically bound to possess accurate and current knowledge about these medications.[13]

Dr Manville presumably has this knowledge, but out of concern and sensitivity to the patient, he may agree to a course of the new medication and absorb the financial loss. If, on the other hand, he continues to refuse and the patient requests enough routine medication to kill himself, Dr Manville should discuss his own ethical approach to the issue of physician-assisted suicide with both the patient and the patient's surrogates. In respecting the patient's wishes, autonomy, and values, the physician is under no obligation to refer a patient explicitly for what he would assess to be an unethical procedure. If the patient is dissatisfied with Dr Manville's response and no longer wants to continue as his patient, Dr Manville is free to provide the patient with a list of other physicians for treatment.

The consensus statement not only supports full, empathic communication with all patients but explicitly identifies terminally ill patients who, for various reasons, are particularly vulnerable to neglect by physicians. The statement does not explicitly discuss physician-assisted suicide, which occurs when a physician facilitates the patient's death by providing either information or the means of the patient's effecting a life-ending act (AMA Code of Ethics: opinion 2.211),[2] but it does obligate physicians to

be well informed about advances in this field. This allows them to competently and sensitively assist dying patients and their loved ones.

In this age of managed care, physicians must guard against "abusing" patients in new ways by allowing them to receive suboptimal treatment.[14] In a recent California case, for example, a physician was charged with "elder abuse" for allegedly failing to adequately treat a dying man's pain.[15] There is evidence that when physicians take the time to inform the patient and family about pain control and other supportive end-of-life measures, the patient usually opts to receive appropriate interventions and to continue receiving care by the treating physician.[16]

CONCLUSION

In this article, we demonstrate an application of the comments and the principles contained in the CMSS consensus statement on the ethic of medicine. The goal is to provide a model for ethical reflection on the problems that arise in everyday practice.

The Council of Medical Specialty Societies staff includes Rebecca Gschwend and Jan Narby.

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Netphiles

We welcome suggestions for Web sites to be included in future Netphiles

Angioplasty

A meta-analysis has shown that although angioplasty for coronary artery disease reduces anginal symptoms in comparison with drug therapy, it seems to do so at the cost of an increased risk of infarction, death, and the need for surgery (*BMJ* 2000;321:73-77).

Both Google (www.google.com) and Altravista (www.av.com) reveal that there are about 10,200 pages with the phrase "coronary angioplasty" on them, a completely unworkable amount of information that hints at the difficulty of getting the results of research into practice. The difficulty of persuading 10,200 authors to revise and update their pages is exceeded only by the difficulty of getting doctors around the world to change their practice.

The pages at www.americanheart.org/Heart_and_Stroke_A_Z_Guide/angioc.html show that almost half a million coronary angioplasties were performed in the United States in 1997 and—whatever the evidence base—an industry like that does not shut down overnight.

Perhaps a certain amount of friction in the system is a good thing: a world in which the publication of a trial 1 day led to an instant revolution in practice the next would be a difficult place in which to live.

Consumer health information about coronary angioplasty is not hard to find. You can download Quicktime movies about having an angioplasty at www.northmemorial.com/nmhc/services/heart/animate.htm. The size of the download will depend on how you set up your Quicktime plug-in (which itself may have to be downloaded). Still, it's worth the wait, with clear animated illustration of the basic anatomic principles and an explanatory soundtrack. And while we're exclaiming at the power of Quicktime, have a look at www.uscuh.com/tour/quicktime/cardiac/cardiac_main.html, a three-dimensional representation of a coronary catheter lab that uses Quicktime VR (virtual reality) to provide a virtual guided tour. Gimmicky perhaps, but used as part of the pre-procedure preparation, it might reduce anxiety.

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CLINICAL EVIDENCE

Eye disorders: bacterial conjunctivitis

This article comes from *Clinical Evidence* (2000;3:305-310), a new resource for clinicians produced jointly by the BMJ Publishing Group and the American College of Physicians–American Society of Internal Medicine. *Clinical Evidence* is an extensively peer-reviewed publication that summarizes the best available evidence on the effects of common clinical interventions gleaned from thorough searches and appraisal of the world literature. It became available in the United States late last year. Please see advertisement for more information or, alternatively, visit the web site at www.evidence.org.

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QUESTIONS: What are the effects of empiric treatment with antibiotics in adults and children with suspected bacterial conjunctivitis? What are the effects of antibiotics in adults and children with culture-positive bacterial conjunctivitis?

INTERVENTIONS

Beneficial

Topical antibiotics (fluoroquinolones, polymyxin B sulfate combinations, aminoglycosides, and fusidic acid [fusidate sodium])

Trade-off

Topical chloramphenicol

DEFINITION

Conjunctivitis is any inflammation of the conjunctiva, generally characterized by irritation, itching, foreign body sensation, and tearing or discharge. Bacterial conjunctivitis may usually be distinguished from other types of conjunctivitis by the presence of a yellow-white mucopurulent discharge. Usually a papillary reaction—small bumps with fibrovascular cores on the palpebral conjunctiva, appearing grossly as a fine velvety surface—is also seen. Bacterial conjunctivitis is usually unilateral, as opposed to viral conjunctivitis that often starts in 1 eye and spreads to the other. This review covers only nongonococcal bacterial conjunctivitis.

INCIDENCE/PREVALENCE

We found no good evidence on the incidence or prevalence of bacterial conjunctivitis.

ETIOLOGY/RISK FACTORS

Conjunctivitis may be infectious (caused by bacteria or viruses) or allergic. In adults, bacterial conjunctivitis is less common than viral conjunctivitis, although estimates vary widely (viral conjunctivitis has been reported to account for 8% to 75% of cases of acute conjunctivitis).[1-3] *Staphylococcus* species are the most common bacterial pathogens, followed by *Streptococcus pneumoniae* and *Haemophilus influenzae*.[4,5] In children, bacterial conjunctivitis is more common than viral and is mainly caused by *H influenzae*, *S pneumoniae*, and *Moraxella catarrhalis*.[6,7]

Summary points

- Bacterial conjunctivitis is usually self-limiting.
- In people with suspected bacterial conjunctivitis, 1 systematic review found limited evidence from 1 randomized controlled trial (RCT) that topical norfloxacin use was associated with a significantly higher rate of clinical and microbiologic improvement than placebo. Comparative RCTs found no significant difference between different topical antibiotics in rates of clinical or microbiologic cure.
- In people with bacterial conjunctivitis proved on culture, RCTs found faster clinical and microbiologic improvement with topical ciprofloxacin and ofloxacin than with placebo. Ofloxacin was associated with reduced relapse rate compared with placebo. Comparative RCTs found no significant difference between topical lomefloxacin and ciprofloxacin in clinical and microbiologic cure rates. One RCT found fusidate sodium to be superior to chloramphenicol.
- Chloramphenicol is the only topical antibiotic possibly associated with serious systemic adverse effects (aplastic anemia).
- We found no trials that examined the potential growth of resistant organisms from the use of antibiotics in bacterial conjunctivitis.

PROGNOSIS

Most bacterial conjunctivitis is self-limiting. In a systematic review of RCTs (primary sources *Cochrane Controlled Trial Register* [updated April 1999], Medline, bibliographies of identified trials, Science Citation Index, and personal contacts with investigators and pharmaceutical companies), 64% of people (99% confidence interval [CI], 54%-73%) had clinical cure or significant improvement on placebo within 2 to 5 days.[8] Some organisms cause corneal or systemic complications, or both; otitis may develop in 25% of children with *H influenzae* conjunctivitis,[9] and systemic meningitis may complicate primary meningococcal conjunctivitis in 18% of people.[10] Conjunc-

tivitis in children is more likely to be bacterial than viral, warranting heightened awareness of possible systemic complications.

AIMS

To achieve rapid resolution of inflammation and to prevent complications with minimal adverse effects of treatment.

OUTCOMES

Time to cure or improvement. **Clinical signs or symptoms:** hyperemia, discharge, papillae, follicles, chemosis, itching, pain, and photophobia. Most studies used a numbered scale to grade signs and symptoms. Some studies also included evaluation by investigators and patients regarding success of treatment. **Culture results:** usually number of colonies, sometimes with reference to a threshold level. Results were often classified into categories such as eradication, reduction, persistence, and proliferation.

METHODS

Clinical Evidence search and appraisal August 1999. All identified systemic reviews and RCTs were reviewed.

Science Photo Library

The left eye of a woman with acute conjunctivitis and periorbital edema

QUESTION: **What are the effects of empiric treatment with topical antibiotics in adults and children with suspected bacterial conjunctivitis?**

One systematic review found limited evidence from 1 RCT that topical norfloxacin was associated with a significantly higher rate of clinical and microbiologic improvement than placebo. Comparative RCTs found no significant difference between different topical antibiotics in rates of clinical or microbiologic cure.

Benefits

Versus placebo: We found 1 systematic review (updated in 1999) that identified 1 RCT comparing the effects of topical norfloxacin use (143 adults) versus placebo (141 adults); 50.4% of participants were culture-positive.[8] Significantly higher rates of clinical and microbiologic cure or improvement at 5 days were obtained with norfloxacin (88.1% [95% CI, 81%-93%] vs 71.6% [95% CI, 63%-79%], $P < 0.01$). **Versus each other:** We found no systematic review. We found 18 comparative RCTs involving adults and children, and these found no significant difference between different topical antibiotics in rates of clinical or microbiologic cure (see table on the Web site www.clinicalevidence.org). Five of the RCTs (evaluating lomefloxacin, fusidic acid, rifamycin, chloramphenicol, and tobramycin sulfate) included grading by patients of effectiveness and tolerability. No significant differences were found.[11-15]

Harms

The placebo-controlled RCT reported minor adverse events in 4.2% of people using norfloxacin and 7.1% using placebo (no statistical analysis available).[5] Placebo contained a higher proportion of benzalkonium chloride (0.01% vs 0.0025% in the norfloxacin solution). One nonsystematic review described complications of topical antibiotic use.[16] These included 4 reported cases of idiosyncratic aplastic anemia associated with topical chloramphenicol and 3 cases of Stevens-Johnson syndrome associated with topical sulfonamides, but no figures were given on the number of people using these drugs.

Comment

The placebo-controlled RCT did not address the effect of using topical antibiotics on antibiotic resistance, which would be of interest given the self-limiting nature of the disease.[5] None of the trials specified their method of selecting participants. The findings may not be generalizable to primary care patients. Most trials included children and adults, and the ratio of children to adults was usually not

specified. Single-blind comparisons were used for lomefloxacin versus chloramphenicol and fusidate and norfloxacin versus fusidate. Lomefloxacin and fusidate are not available in the United States, and chloramphenicol is rarely used in the United States because of reports of idiosyncratic aplastic anemia.

QUESTION: What are the effects of topical antibiotics in adults and children with culture-positive conjunctivitis?

Randomized controlled trials in people with bacterial conjunctivitis proved on culture found faster clinical and microbiologic improvement with the use of ciprofloxacin, ofloxacin, or the combination of polymyxin B sulfate and bacitracin zinc than with placebo. The use of ofloxacin was associated with reduced relapse rates. Comparative RCTs found no significant difference between tobramycin and ciprofloxacin or between the combination of trimethoprim and polymyxin B sulfate and sulfacetamide sodium in clinical and microbiologic cure rates. One RCT found greater clinical efficacy and less microbiologic resistance with fusidate than with chloramphenicol.

Benefits

Versus placebo: We found 1 systematic review (updated 1999) that identified 3 placebo-controlled RCTs evaluating polymyxin-bacitracin, ciprofloxacin, and ofloxacin in bacterial conjunctivitis proved by culture. The review identified no trials of gentamicin sulfate that included only culture-proven conjunctivitis.[8] One RCT of children (n = 84)[17] found that in culture-proven *H influenzae* and *S pneumoniae* bacterial conjunctivitis, a higher clinical cure rate at days 3 to 5 was seen with polymyxin-bacitracin than with placebo, although by days 8 to 10, the difference was not significant (62% vs 28% at days 3-5 [$P < 0.02$], and 91% vs 72% at days 8-10 [$P > 0.05$]). The microbiologic cure rate was significantly higher with antibiotics at days 3 to 5 and 8 to 10. When antibiotics were given parenterally for concurrent problems, no significant difference was found between groups, but the numbers were too small to rule out a clinically important difference. Two other trials identified in the review did not specify the age of participants. One did not evaluate clinical outcome but found significantly greater microbiologic improvement at day 3 in people treated with ciprofloxacin (n = 177).[18] One RCT published as an abstract only found significantly greater clinical and microbiologic improvement at day 2 in people treated with ofloxacin (n = 132): 64.1% versus 22.1% improved at day 2 ($P < 0.001$). It also found a lower relapse rate in people treated with ofloxacin 2 days after treatment stopped.[19] A 4th trial was published in the Japanese language and was not reviewed.[20]

Versus each other: We found no systematic review. We found 1 RCT that did not specify the age of participants and 3 RCTs in children only. The former found no significant difference in microbiologic eradication or improvement between ciprofloxacin (n = 140) and tobramycin (n = 111); eradication or improvement occurred in 94.3% versus 91.9% ($P > 0.5$ [no CI available]).[18] Clinical cure was not evaluated. Of the 3 RCTs in children, 2 found no significant difference in clinical or overall microbiologic efficacy between ciprofloxacin and tobramycin (n = 70 vs 71 [eradication, 90.1% vs 84.3%, $P = 0.29$; cure, 87% vs 89.9%, $P = 0.6$]) or between trimethoprim-polymyxin B, gentamicin, and sulfacetamide (n = 53 vs 57 vs 46 [eradication, 83% vs 68% vs 72%, $P > 0.1$; cure, 84% vs 88% vs 89%, $P > 0.1$]).[21,22] The third (non-blinded) RCT found more clinical efficacy and less microbiologic resistance with fusidate than with chloramphenicol (n = 114 vs 25 [cure, 85% vs 48%, $P < 0.001$; resistance, 16% vs 55%, statistical analysis not provided]).[23]

Harms

Of the 116 children initially enrolled in the first RCT described above, 1 was excluded because of possible allergic reaction to the ointment; the other exclusions were unrelated to adverse effects.[17] In RCTs that included people with both culture-proven and suspected bacterial conjunctivitis, minor adverse events were reported with antibiotics: burning, bitter taste, pruritus, or punctate epithelial erosions (35% with tobramycin vs 20% with ciprofloxacin; no statistical detail available from abstract)[24]; bad taste (20% with norfloxacin vs 6% with fusidate)[25]; and stinging (50% with norfloxacin vs 37% with fusidate) and burning (gentamicin more than lomefloxacin).[13]

Comment

None of the RCTs addressed the effect on antibiotic resistance of using topical antibiotics in bacterial conjunctivitis, which would be of interest given the self-limiting nature of the disease. Furthermore, they did not report on patient-oriented outcomes or look at rates of reinfection.

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Culture and Medicine

White coat ceremonies for new medical students

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Earlier this year, I attended my first white coat ceremony for incoming medical students. So impressed was I by the event that I feel impelled—almost duty bound—to spread the word, for few outside of academia are likely to have heard of these ceremonies.

Essentially, they are a rite of passage, welcoming the new medical student into the medical profession, albeit as an apprentice member. They occur right at the beginning of medical school, before the students have taken any lectures or laboratory classes, and the students' families and friends are invited by the medical school to attend. The students are congratulated on their achievement in being selected as medical students, and told about the commitment that, as student doctors, they are making both to becoming and staying proficient in the science and technique of medicine and also to the human obligations of being a doctor—especially to the central obligation of caring for their patients. (The brochure at the ceremony I attended quoted from an eminent American physician of the 1930s, William Peabody: "The secret of caring for the patient . . . is caring for the patient!"—not a bad message on its own for the new medical student to take away.) A physician with some special interest and/or skill in medical humanities gives a lecture, welcoming the new students and emphasizing the importance of the human side of medicine and the importance of integrating it into the science and technology of medical practice.

In the ceremony I attended, after all, including the medical faculty, had taken their seats in the auditorium, everyone then stood as the new students were led in procession to take their seats. A doctor who was selected by the students and faculty then talked about his experiences in medicine at that medical school and his subsequent career. The visiting speaker, a physician with a specal interest in medical ethics, then gave a half-hour talk in which he linked the goals of medicine with the ethics of medicine, asking his audience never to forget to reflect on what the purposes of being a good doctor were. He urged them to be proud of the fact that the core objective of doctors was to do good for the health of the people they served. He explored the relationship of trying to do good and the ancient obligation of *"primum non nocere,"* as well as contemporary concerns both for respect for people's autonomy ("apart from other considerations, it's far easier to do good for people if you know and honor their values and aspirations") and justice ("the need to meet competing claims fairly—including claims on you").

After the white coat lecture came the "robing ceremony." All 250 or so new medical students had been presented with a short white coat by the medical school and, as each student's name was called by a senior member of the faculty, several others including the dean of medicine, and doctors from the school who were well respected for their commitment to the humane aspects of medicine, as well as the white coat lecturer, helped each student into his or her new coat—murmuring words of congratulations and good luck as they did so—sometimes vigorously assisted by cheering from the particular student's family and fans. Then, the students stood and, led by one of the school's senior staff, read an affirmation of "professional commitment." They promised to pursue diligently their medical education and training from that day until they retired from medical practice; to put the interests of their patients before their own; to respect and value their fellow health professionals; to be tolerant, compassionate, and honest; to respect, support, and encourage their classmates, now their colleagues; to adhere to the university's

honor code; and to behave well and honorably throughout their medical careers, always striving to be worthy of the privilege of being a doctor and never abusing it. All students then processed out to a sumptuous reception given by the medical school for the new students and their families and friends. When, as an outside observer, I discreetly asked some of the students afterwards what they thought of the ceremony—"what you really thought of it please!"—the small but random sample whom I asked had all been deeply impressed and pleased by it and were unanimous in their praise for it.

I have to say that starting from a position of indifferent skepticism, I have changed into an enthusiastic supporter of the white coat ceremony. Medical professional life does indeed start at the beginning of medical studies, not at qualification—medical students are bound by at least some of the same professional commitments that bind all doctors (a few examples are the commitments to medical confidentiality, to working for the good of the patients and avoiding harming them, and not to exploit their quasi-professional privileges, for example by taking sexual advantage of patients). Explicitly enrolling students into the profession welcomes them, affirms their new status and emphasizes—at a highly impressionable stage of their careers—the importance of committing themselves to excellence, not only in the scientific and technical areas of medicine but also in its human and humanitarian aspects. Medical school deans and their colleagues throughout the world are warmly recommended to consider the possibility of introducing a white coat ceremony at their own school!

*The Arnold P Gold Foundation is at 260 Lincoln Street, Englewood, NJ 07631.

Medical myth: A digital rectal examination should be performed on all individuals with possible appendicitis

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The digital rectal examination is uncomfortable, and it can be emotionally and physically traumatic, especially in children. Dickson and Mackinlay found that rectal examinations induced severe discomfort, defined as major crying and screaming, in nearly one third of all children presenting with possible appendicitis.[1] Mild discomfort, defined as facial grimacing or crying, was seen in another third of this group of patients.

The routine use of digital rectal examination has long been considered a necessary component in the evaluation of patients in whom appendicitis is suspected. This traditional teaching is still supported in most surgical textbooks. The 19th edition of *Cope's Early Diagnosis of the Acute Abdomen* states that the rectal examination is extremely important and informative because it can elicit tenderness from an inflamed and swollen appendix.[2] Contrary to this traditional teaching, results of several studies suggest that subjecting patients to this unpleasant examination will likely add nothing to the diagnosis or management of the patient suspected of having appendicitis.

In 1979, Bonello and Abrams performed a limited retrospective analysis of rectal examinations in 495 patients undergoing surgery for possible appendicitis.[3] The results of the rectal examinations were positive in only 46% (228/495) of those patients with confirmed appendicitis. Fifty-three percent (262/495) of patients without appendicitis had false-positive results. The authors concluded that the rectal examination does not confirm or rule out the diagnosis of acute appendicitis.

Dickson and Mackinlay prospectively evaluated children 14 years of age or younger who were admitted to the hospital with suspected acute appendicitis.[1] A positive rectal examination was defined as tenderness of the right or anterior rectum, the presence of swelling, or the presence of a mass. Again, the rectal examination was insensitive; only one half of the patients with documented acute appendicitis had positive results of rectal examinations. Furthermore, it was concluded that in 90% of cases, the diagnosis could have been rendered on the basis of the history and results of the abdominal examination alone. The authors state that rectal examination should not be performed in children with possible appendicitis unless the diagnosis remains uncertain after taking the history and examining the abdomen.

The largest study of the use of rectal examinations in patients with possible appendicitis was performed by Dixon and colleagues in 1991.[4] Of 1204 patients, ranging in age from 7 to 87 years, with a chief complaint of right lower quadrant pain, 85% (1024/1204) underwent a rectal examination. The treating physicians were asked to render their diagnosis and disposition plan after taking a history and conducting a physical examination, but before they did a rectal examination. The same physicians were asked to give their diagnosis and disposition after the rectal

examination. The rectal examination made no difference in the management plan for any of the patients. The data suggested that physical signs, most importantly abdominal rigidity, were better predictors of appendicitis. The finding of right-sided rectal tenderness was ultimately neither sensitive nor specific for the disease. The authors concluded that a rectal examination is not necessary in patients with right lower quadrant abdominal pain and physical signs.

Scholer and colleagues published a limited retrospective study of rectal examinations in children ranging in age from 2 to 12 years presenting with abdominal pain.[5] Of 1140 patients, only 5% (56/1140) underwent a rectal examination. The examination was only deemed contributory—undefined in the study—in 12 of the 56 patients (21%). Only 25% (2/8) of patients with appendicitis had lateral wall tenderness at the time of the examination. It is unclear from the study if this finding added to the ultimate diagnosis or management of the patients.

The results of the studies just described suggest that the rectal examination should not be considered part of the *routine* work-up of right lower quadrant abdominal pain because it has little utility in guiding the diagnosis or management of possible appendicitis; it is uncomfortable; and, especially in children, it may be traumatic and poorly tolerated. The rectal examination may be deemed necessary when alternative diagnoses are likely. The examination should then be used judiciously to rule out specific conditions, including gastrointestinal bleeding, prostatitis, a mass, or perirectal abscess.

As stated by Jesudason and colleagues, the rectal examination should be considered an "investigation" rather than part of a routine clinical assessment.[6] It should be performed only when the results will change the management plan.

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Toolbox

Acute stroke

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Acute stroke is now a treatable condition that warrants urgent specialist attention. Drug treatment and specialist care both influence survival and recovery. In this article, we consider the optimal approaches to diagnosis and early management.

Stroke, a sudden neurologic deficit of presumed vascular origin, is a clinical syndrome rather than a single disease. A common and devastating condition, it causes death of one third of patients at 6 months (table 1) and leaves another third permanently dependent on the help of others. Each year in the United Kingdom, 110,000 cases of first strokes and 30,000 cases of recurrent strokes occur; 10,000 strokes occur in people younger than 65 years, and 60,000 people die of stroke. It is the largest cause of disability, and more than 5% of National Health Service and social services resources are consumed by stroke patients. Correct management relies on rapid diagnosis and treatment, thorough investigation, and rehabilitation.

Conditions requiring referral to a hospital

Admit to hospital

- Neurologic deficit lasting 1 hour or more
- Dependent patient—that is, moderate to severe stroke
- Transient ischemic attack lasting 1 hour or more
- More than 1 transient ischemic attack within a week
- Transient ischemic attack while on anticoagulation therapy
- Patient presenting to a hospital
- At request of general practitioner

Refer to cerebrovascular clinic

- Independent patient more than 48 hours after stroke; withhold aspirin
- Transient ischemic attack lasting less than 1 hour; give aspirin

Symptoms and signs of stroke

Anterior circulation strokes

- Unilateral weakness
- Unilateral sensory loss or inattention
- Isolated dysarthria
- Dysphasia
- Vision:
  Homonymous hemianopia
  Monocular blindness
  Visual inattention

Posterior circulation strokes

- Isolated homonymous hemianopia
- Diplopia and disconjugate movement of eyes
- Nausea and vomiting
- Incoordination and unsteadiness
- Unilateral or bilateral weakness and/or sensory loss

Nonspecific signs

- Dysphagia
- Incontinence
- Loss of consciousness

ASSESSING THE PATIENT

Patients should be assessed at a hospital immediately after a stroke. They may need to go straight to the hospital rather than wait to see their general practitioner because treatments such as thrombolysis must be administered within as little as 3 hours after stroke. Ambulance crews can be trained to apply simple screening questions to identify patients who are likely having a stroke.

Stroke is a clinical diagnosis, but brain imaging is required to distinguish ischemia from primary intracerebral hemorrhage. The pattern of neurologic signs, including evidence of motor, sensory, or cortical dysfunction and hemianopia, can be used to diagnose certain clinical subtypes and thus to predict prognosis (table 2). Other signs also relate to outcome and may help identify the cause. If neurologic symptoms resolve within 24 hours, the traditional diagnostic term is "transient ischemic attack" rather than stroke. However, not all transient ischemic attacks are genuinely ischemic; many are associated with permanent cerebral damage. A better term, therefore, is "ministroke."

Table 1 *Death rate (percentage) 30 days, 1 year, and 5 years after different types of stroke*

Stroke type	30 days	1 year	5 years
Ischemic stroke	10	23	52
Intracerebral hemorrhage	52	62	70
Subarachnoid hemorrhage	45	48	52

PATHOPHYSIOLOGY

For practical purposes, there are 2 types of stroke after subarachnoid hemorrhage has been excluded. Ischemia accounts for 85% of presentations and primary hemorrhage for 15%. Hemorrhage causes direct neuronal injury, and the pressure effect causes adjacent ischemia. Primary ischemia results from atherothrombotic occlusion or an embolism. The usual sources of embolism are the left atrium in patients with atrial fibrillation or

Clinical examination after stroke

- Conscious level
- Neurologic signs
- Blood pressure
- Heart rate and rhythm
- Heart murmurs
- Peripheral pulses
- Systemic signs of infection or neoplasm

Table 2 *Characteristics of subtypes of stroke*

Characteristic and prognosis	Lacunar	Partial anterior circulation	Total anterior circulation	Posterior circulation
Signs	Motor or sensory only	2 of following: motor or sensory; cortical; hemianopia	All of: motor or sensory; cortical; hemianopia	Hemianopia; brain stem; cerebellar
Dead at 1 year, %	10	20	60	20
Dependent at 1 year, %	25	30	35	20

the left ventricle in patients with myocardial infarction or heart failure.

Vessel occlusion arises from atherosclerosis, typically in the internal carotid artery just above the carotid bifurcation or from small vessel disease deep within the brain. Ischemia causes direct injury from lack of oxygenation and nutritional support and sets up a cascade of neurochemical events that lead to spreading damage. The ischemia may be reversible if reperfusion is obtained quickly (now proved in clinical trials), and the chemical injury may be interrupted by various neuroprotective drugs (unproved in humans).

EMERGENCY MANAGEMENT

Within the first hours after the onset of cerebral ischemia, part of the brain is under threat of death. The infarct core may be densely ischemic and will inevitably die, but tissue with a compromised blood supply is also balanced on a knife edge between death and recovery. At this stage, oxygenation and hemodynamic and metabolic factors are crucial. The emergency management of stroke requires medical stabilization and assessment of factors that may lead to complications (such as swallowing and hydration); thrombolysis may be considered (discussed later). An acute stroke unit concentrates patients, health care staff, resources, and expertise into 1 area, and such units may be associated with a better outcome.

INVESTIGATIONS

Patients with acute stroke should have computed tomography of the brain to distinguish ischemic from hemorrhagic stroke (figures 1 and 2). This separation is vital because subsequent investigations and treatment differ for the 2 types. Neuroimaging will also identify conditions that mimic stroke (table 3) and can help predict outcome. Ideally, imaging will be performed soon after admission. Magnetic resonance imaging of the brain may eventually replace computed tomography because it not only identifies stroke anatomy but can also assess blood flow and perfusion in the brain, detect whether lesions are new or old, and identify carotid artery stenosis (figure 3).

The extent to which the cause of the stroke should be investigated depends on several factors, including the likely degree of recovery, the presence of obvious risk factors, and the age of the patient. Younger patients are more likely to have an identifiable cause such as an inflammatory or clotting disorder that may require specific treatment. Although

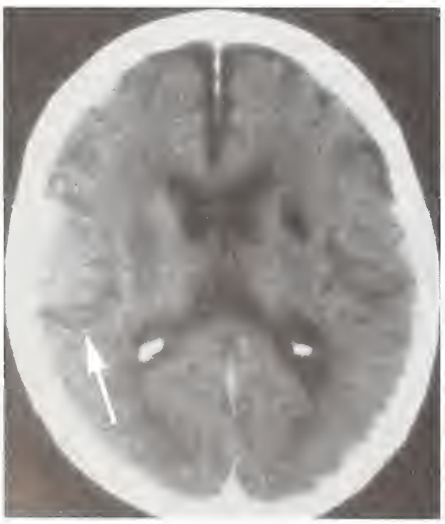

Figure 1 Computed tomographic scan showing ischemic stroke

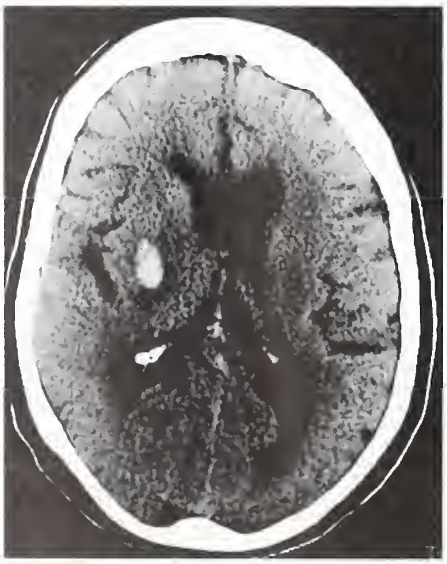

Figure 2 Computed tomographic scan showing hemorrhagic stroke

Table 3 *Conditions that mimic stroke*

Diagnosis	Diagnostic features
Decompensation of previous stroke	Evidence of infection such as urinary or respiratory tract; metabolic disturbance
Cerebral neoplasm (primary or secondary)	Less abrupt onset; primary tumor or secondary to, for example, lung or breast cancer
Subdural hematoma	Recent head injury
Epileptic seizure	Possible previous episodes
Traumatic brain injury	History of trauma
Migraine	Less abrupt onset; followed by headache; younger patients
Multiple sclerosis	Less abrupt onset; possible previous episodes
Cerebral abscess	Infection

Investigation of stroke

All patients
- Computed tomography (or magnetic resonance imaging)
- Electrocardiography
- Chest radiography
- Complete blood cell count
- Clotting screen
- Electrolyte and creatinine concentrations

Subgroups
- Carotid duplex scanning
- Echocardiography
- Thrombophilia screen
- Immunology screen
- Serologic test for syphilis
- Cerebral angiography (rarely)

Figure 3 Magnetic resonance angiogram showing middle cerebral artery occlusion

Complications of stroke

Hyperglycemia

Hypertension

Fever

Infarct extension or rebleeding

Cerebral edema, herniation, coning

Aspiration

Pneumonia

Urinary tract infection

Cardiac dysrhythmia

Recurrence

Deep venous thrombosis, pulmonary embolism

investigations should be restricted to tests that will inform clinical management, guidelines can be used to determine which investigations are needed after stroke.

SWALLOWING AND FEEDING

Dysphagia affects 35% of stroke patients. It is often unrecognized after mild stroke and is associated with a poor outcome, partly because it predisposes to aspiration and pneumonia and partly because of the nutritional deficit. The presence of a gag reflex is a poor guide to safe swallowing, and a formal assessment by trained staff is essential. Fluids are more difficult to swallow than semisolids.

Acute drug therapies for ischemic stroke

Aspirin
- Most patients
- Heparin (unfractionated or low molecular weight)

Prophylactic
- Previous venous thromboembolism
- Morbid obesity

Therapeutic
- Carotid artery dissection
- Embolic, recurrent transient ischemic attacks

Dysphagic patients should be fed through a nasogastric tube or percutaneous endoscopic feeding tube until it is safe to resume oral food and fluids. Most dysphagic patients will not need enteral feeding beyond a few weeks. However, when and how optimally to feed dysphagic patients remain to be determined.

ACUTE INTERVENTION

Firm evidence from 2 large trials has shown that a regimen of aspirin (160-300 mg daily by mouth, nasogastric tube, or rectum) started within 48 hours of the onset of acute ischemic stroke reduces the risk of subsequent disability and death. However, the effect of aspirin is small (number needed to treat [NNT] = 77) and is principally mediated through reducing the risk of early reinfarction. Neuroimaging is strongly recommended before starting the aspirin regimen. A large trial of the use of unfractionated heparin in stroke patients found that heparin did not improve outcome, even in patients with presumed embolic stroke. Recently, low-molecular-weight heparin has proved ineffective in individual large trials and meta-analysis. Heparin may still be useful in certain groups of patients.

Thrombolysis with alteplase recombinant within 3 hours of the onset of stroke significantly increases the chance of a nearly complete recovery (NNT = 7) when administered by specialists (figure 4). Treatment up to 6 hours after a stroke has been less effective in meta-analysis of randomized controlled trials (estimated NNT = 12). Thrombolysis is currently licensed for use in stroke only in North America, and concerns remain about its safety if used indiscriminately.

Neuroprotectant drugs (which may protect neurons from ischemia) have to date shown no benefit in ischemic or hemorrhagic stroke, although several trials are still in progress.

Patients with a large cerebellar infarct or hemorrhage should be referred for immediate neurosurgical evaluation to facilitate evacuation of the clot or infarct or shunting for acute hydrocephalus, if required. Anticoagulant therapy should be reversed in patients with primary intracerebral hemorrhage.

COMPLICATIONS OF STROKE

Stroke may be complicated by several conditions that can alter outcome adversely. Hyperglycemia, fever, and hypertension are each associated with a poor prognosis. In the absence of trial evidence, increased glucose concentrations should be normalized and paracetamol [acetaminophen] given for fever (figure 5). In contrast, hypertension should not be treated for the first week because some antihypertensive drugs (notably calcium channel blockers) seem to worsen outcome, possibly be reducing regional cerebral blood flow. Large ischemic strokes are often complicated by edema, swelling, and herniation,

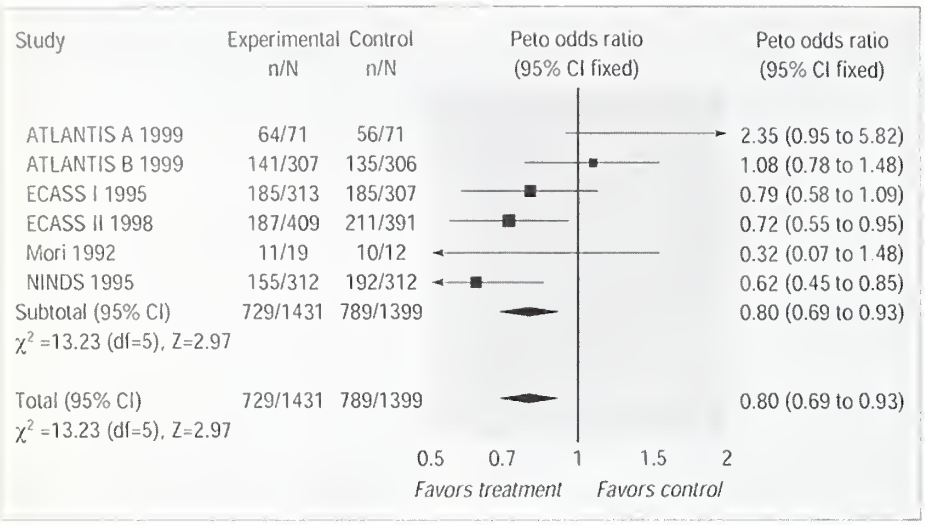

Figure 4 Meta-analysis shows that thrombolysis reduces combined disability and death from stroke

leading to death; no proven treatment is available for these complications.

Venous thromboembolic disease (deep venous thrombosis, pulmonary embolism) develops in half of immobile patients unless preventive measures are taken. Although compression stockings reduce the risk of deep venous thrombosis in other groups of high-risk patients, this has not been confirmed in patients with stroke. A combination of stockings, early mobilization, adequate hydration, and aspirin is considered good practice in patients with ischemic stroke. Early mobilization may also reduce the risk of pressure sores and respiratory and urinary tract infections. When possible, the use of urinary catheters should be avoided to minimize the risk of infection.

REHABILITATION

The principal aims of rehabilitation are to restore function and reduce the effect of the stroke on patients and their care givers. Rehabilitation should start early during recovery with assessment and mobilization while the patient is in the acute stroke unit. Once patients are medically stable, they should be transferred to a stroke rehabilitation unit if further rehabilitation is required. Formal rehabilitation in a stroke unit is associated with reduced incidences of disability and death (NNT = 12) and a shorter stay in the hospital. Optimal care is multidisciplinary: physicians, nurses, physiotherapists, occupational therapists, speech and language therapists, dieticians, psychologists, and social workers all have a role.

Figure 5 Stroke patient receiving rehabilitation therapy

SECONDARY PREVENTION

Secondary prevention (apart from blood pressure control) should start shortly after admission. All patients should be offered lifestyle guidance, including advice to stop smoking, reduce saturated fat and salt consumption and alcohol intake, lose weight, and increase exercise. Aspirin therapy started for the treatment of acute ischemic stroke should be continued indefinitely for secondary prevention. The use of alternative or additional antithrombotic drugs—dipyridamole, clopidrogrel bisulfate, and warfarin sodium—carotid endarterectomy, and management of hypertension and hyperlipidemia after stroke is discussed elsewhere (*BMJ* 2000; 320:991-994).

THE FUTURE

Stroke management is now supported by solid evidence, but many questions remain unanswered. Whenever possible, patients should be given the opportunity to enroll in randomized trials of acute interventions, rehabilitation, or secondary prevention.

The magnetic resonance image was provided by Professor Alan Moody, University of Nottingham. The data on thrombolysis were provided by Dr Joanna Wardlaw, University of Edinburgh.

Further reading

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West of the Rockies

Letter from Abroad

Medical training under fire

The Mae Tao medical school on the Thai-Burma border

Jamie Saben

Correspondence to: Dr Saben jamsab@ucla.edu

> "I can do episiotomies, suture wounds and deliver babies now...but the hardest part is that I need to learn more. . . . If you stop learning, then you stop living." *Tah Bo, junior medic*

Imagine learning to practice medicine in 1 year, in a language you only partially understand. Picture returning to your jungle refugee camp, or perhaps the front line, where patients with high fevers and rigors look to you for a cure.

These are the lives of Burmese refugee medics. I spent 3 weeks with them in October of 1999 during an elective at the Mae Tao clinic on the border between Thailand and Burma. The creation of this clinic, a de facto medical school, was spurred by Burma's political turmoil.

In the summer of 1998, 60 students arrived at the Mae Tao clinic for intensive medical training. They came by foot, truck, or plane from the 9 refugees camps scattered up and down the Thai-Burma border. A few trekked for days from their villages in Burma just to be trained by Dr Cynthia Maung, who is widely known as a selfless physician dedicated to helping her people.

Most of these journeys were sponsored by nongovernment organizations, which are assisting with developing an infrastructure and other activities in the camps, or by the Karen National Union, a political group battling with the current Burmese military junta for control of the Karen state in Burma. A few students were sponsored by individual benefactors working in the camps; others arrived on their own, unannounced. Dr Cynthia warmly welcomed them all. For the 6 years that the medic training program has existed, she has never charged tuition.

These young medics grew up in conditions that would shock westerners. Their families were among the hundreds of thousands forced from their homes in Burma by oppressive military rule. They moved to border refugee camps, many of which have been attacked or burned at least once. Everyone here knows someone who has been beaten, raped, or killed. And now the students have chosen a 1-year crash course in medicine in order to better help their fellow refugees.

When she first established the clinic in 1989, Dr Cynthia treated patients with war wounds and malaria with the assistance of a small staff. Some university students who fled Burma in the late 1980s and early 1990s came to help the refugee patients at the clinic and to learn from Dr Cynthia. At that time, medical instruction was largely informal, and the students learned on the job.

The first class of medics graduated in 1994 with less than 40 students. "Each year, the number [of students] has increased, as has the quality of the students attending," said

Tah Bo administers oral polio vaccine at a nearby refugee camp

Htoo Paw examines a patient while a new medic watches and learns

senior medic Htat Aung, a former university student who teaches public health.

An Australian teacher working in Mae Ra Moo camp sponsored 20-year-old Htoo Paw to make the 7-hour trip to the clinic in the back of a truck. She began classes on the day of her arrival. "It was a new experience," she said in her quiet English. "I met people from other places . . . we had different culture problems, but we tried to negotiate with each other."

Aside from their different religious backgrounds, many of the students are of Karen ancestry, a minority group in Burma, while others are Burmese. This diversity is a source of conflict. The Karen are indigenous to Southeast Asia, and by most historical accounts, they are the original settlers of where Burma stands today. Centuries ago, these traditionally peaceful, devout farmers were driven from their homes or enslaved by the Burman (ethnic Burmese), who won the feudal war for control of the area. In the 20th century, the Burmese government has repeatedly denied the Karen request for a self-determined state. The Karen united with other ethnic minority groups in Burma to form the National Democratic Front in opposition to the ruling government. Even though the Burmese military government persecutes the ethnic minorities and economically disadvantaged Burman alike, unspoken tensions still exist between the Karen and Burmese students.

Classes are taught in Burmese, which makes it difficult for the Karen who have their own language and who learned Burmese in high school as a second language. "There is still a problem with the different languages," said Dr Cynthia. "Next year we will have some more people who speak Karen and can help tutor students at night."

After graduating, the students' lives may never cross paths again. Some, like Htoo Paw, leave within weeks to fulfill their obligations to their sponsors by returning to the camps. Others, like Tah Bo, remain behind to gain practical experience in the clinic before leaving. In the camps, some medics will work under a volunteer doctor's supervision, while others will be virtually alone in their practice.

Some students will be sent to the front lines in the jungle to help Karen National Union soldiers. Those who come to the clinic without a sponsor are allowed to stay for 2 to 3 years. The newly graduated medics can treat a range of conditions, such as endemic infections, trauma, and malnutrition. They can also deliver babies. The medicine they practice is far from perfect, but in this war-torn area, brief medical training is better than none.

As for the future of the program, many questions remain. Should there be a limit on the number of medics trained per year? If so, is an entrance examination necessary to screen for minimal intellectual requirements? And should students be able to get specialized training in certain subjects? In answer to this last question, Dr Cynthia replied: "We teach primary care medicine here. As patients develop more severe health problems, like HIV, tuberculosis, and severe malaria, the specialized training needs to increase. Also, the demand from nongovernment organizations to train medics for the camps continues to grow."

The conflict in Burma is likely to continue indefinitely, creating the need for new generations of medics who will be prepared to help their fellow refugees.

For more information about Dr Meung's clinic, or to make a donation, contact: The Allende Program in Social Medicine, 520 Washington Blvd #380, Marina del Rey, CA 90292.

capsule

Does yogurt have healing properties? The *American Journal of Clinical Nutrition* recently devoted 10 closely printed pages, including 162 references, to the healing properties of yogurt (*Am J Clin Nutr* 2000;71:861-872). The conclusion of this dense and difficult review is that yogurt might be good for the immune system. But then again, it might not. We won't know, say the authors, until yogurt investigators stop studying mice and start studying humans.

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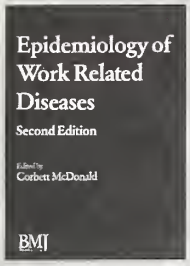

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Critical Care
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The theatre of medicine

David Heiden

Neighbors watching a "house call" for a patient with malaria. Boo'co Refugee Camp, Somalia, 1982

The drama of a doctor's work fascinates people. Something real and important is at stake. There's mystery, and an uncertain outcome. When a doctor works in an accessible real-life setting, at a street-corner accident or a house call, everyone tries to crowd around.

In the refugee camp, we worked in public view. Doctors did the same thing several generations ago in America, when most births and deaths occurred at home. In *The Doctor Stories,* William Carlos Williams even describes an "appendix operation" performed on the kitchen table.

These days, people usually see medicine on TV and not the real thing. When doctoring is done well on TV programs, from *Dr Kildare* and *Marcus Welby* to *ER* and *Chicago Hope,* there are usually good ratings. But something is lost because the real thing is inaccessible. Fantasy and exaggeration replace reality in a way that seems sadly consistent with the rest of our culture.

David Heiden is an ophthalmologist practicing in San Francisco

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This month in wjm

Children can be taught to behave safely around strange dogs

Dog bites are a major cause of injury in children. In the United States, there are more than 300,000 emergency department visits for dog-bite injuries each year. Boys aged 5 to 9 years are particularly at risk. But can children be taught to avoid being attacked by dogs? In a randomized controlled trial, Chapman and colleagues found that a brief lesson from a dog handler increased the precautionary behavior of young children around strange dogs (page 233). But it is uncertain, says Grossman in a commentary on page 234, whether this behavioral change will translate into fewer bite injuries.

Claims that plant estrogens are beneficial are unsupported

Plant estrogens—found in soy products—are promoted by health food stores as a "natural alternative" to hormone replacement therapy. But in a curbside consult on page 272, Gibaldi says that there is no evidence to suggest that these phytoestrogens have beneficial clinical effects. The isoflavones in soy products have also been associated with cancer.

Poor communication leads to grievances against physicians

Patients have become increasingly empowered and, therefore, more likely to complain when they are dissatisfied with their physician. But what leads to this dissatisfaction? In a retrospective review of 11 years' experience with a medical society's grievance committee, Halperin found some answers (page 235). Complaints about physicians included that they were rude and that they failed to make a prompt diagnosis. Inadequate communication was at the root of many complaints. Patient grievances are "a continuing challenge for medical science," says Localio on page 239.

Guidelines may help to reduce deaths from meningitis

Nearly 1 in 4 adults with acute bacterial meningitis die, and many survivors are left with chronic disabilities. The prognosis is worse if there is a delay in management, and so the outcome depends on whether the attending physician suspects the diagnosis and whether the health care system is set up to aid rapid diagnosis and therapy. Standardized guidelines for management are invaluable, argue Møller and Skinhøj in an Op-Ed on page 223. Those recently issued by the British Infection Society may provide a template for use by physicians in other countries.

Physicians can learn ways to notify relatives about sudden deaths

After the sudden death of a patient, it is often up to the physician to break the terrible news to the relatives. But the "survivors" have had no time to prepare for their loss, and the task of telling them is often terrifying. Iserson reviews the ways in which physicians can remain compassionate while notifying survivors (page 261). Using nonmedical language is important, as is showing that you care that their loved one has died. Protocols can help notifiers to prepare for their task and to understand what to expect.

Editor's pick

Rural America has 20% of the nation's population but only 10% of its physicians. This uneven distribution is just one of the ways in which rural people receive a poor deal when it comes to health care. Kim surveyed health care providers working in the Navajo Area Indian Health Service and found that half were planning to leave within the next 3 years (page 240). In a commentary on page 243, Chilton argues that employers in rural areas need to do more to retain physicians, including improving their housing and providing better facilities for their families.

But why is it that doctors need incentives to work in disadvantaged areas? Perhaps part of the problem is the way in which students are chosen for entry to medical school. Studies have shown that there is a bias toward choosing students from affluent backgrounds. These students are accustomed to the trappings of economic and social success. So when they qualify, it is no surprise that many choose the highest-earning specialties in metropolitan areas. The inner cities and the poorest rural regions remain poorly served.

The mismatch between the social makeup of patients and their physicians has other implications. The burden of ill health falls on the poorest sectors of society, yet their health care providers are among the wealthiest. This leaves physicians unable to understand and empathize with their patients' experiences. Add to this the growing ethnic and cultural diversity of our patients—many of whom speak little English—and you have a major disconnect between patient and provider.

The medical profession needs to be more representative of the society it serves. Medical schools must reach out to marginalized communities and actively encourage candidates from a wide variety of backgrounds. We need more programs like Medicos para El Pueblo in Los Angeles, which aims to increase the number of Latino students applying to study medicine. If we fail to narrow the social gap between doctors and patients, then the very foundation of medicine—the ability to truly serve those in need—will eventually disappear.

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Op-Ed

The epidemic of pediatric obesity

Perspectives and approaches for primary care

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Most people do not need statistics to notice the fattening of our population, especially our children. In the United States across all ethnic groups and socioeconomic strata, the prevalence of pediatric obesity has doubled in the past 2 decades.[1] Childhood obesity is both an immediate and future health problem. Sixty percent of overweight children already suffer from hypertension, hyperlipidemia, and/or hyperinsulinemia.[2] Increased obesity has led to a new epidemic of type 2 diabetes mellitus in children and adolescents,[3] and autopsy studies of children who died of traumatic causes show that early atherosclerotic lesions are already developing in the aortas and coronary arteries of overweight children.[4]

The first step for primary care physicians is to identify children at risk. The Centers for Disease Control and Prevention has recently released revised growth charts that are more representative of the US population and include body mass index (BMI) curves for boys and girls from age 2 to 20 years (http://www.cdc.gov/growthcharts/). The BMI is calculated as the weight in kilograms divided by the square of the height in meters: weight (kg)/[height (m)]^2. The BMI is the most appropriate measure to use in the clinical setting.[5] Children above the 85th percentile of the BMI growth curves should be considered at risk for overweight, and children above the 95th percentile should be considered overweight. Detailed recommendations for medical evaluation for overweight children are also available.[6]

Overweight children and adolescents are at significantly greater risk of adult obesity. Historical data suggest that the risk for adult overweight is primarily influenced by 2 factors. The first is age: overweight in 0- to 5-year-olds is only minimally predictive of adult overweight; less than half of overweight prepubertal children have become overweight adults, whereas as many as 70% to 80% of overweight teens have become overweight adults. The second is parental overweight: children with overweight parents, regardless of child's weight, are at increased risk of becoming overweight adults. Overweight children at greatest need of treatment, therefore, are those who are already manifesting an obesity-associated morbidity—hypertension, hyperlipidemia, hyperinsulinemia, diabetes, or poor self-esteem or depressive symptoms due to their weight—and those who are overweight beyond puberty, have 1 or more overweight parents, or both.[7]

Pediatric obesity treatments have been far from uniformly successful, although childhood treatment has produced better long-term results than adult treatment. The current state-of-the-art is intensive, family-based, group behavioral programs. In some studies, these programs have produced 10-year success in up to 30% of children.[8] Unfortunately, state-of-the-art group programs are not available in most communities, but they have features that can be adopted by clinicians.[9] These include involving parents—and other family members—in treatment, allowing changes in the home environment and social support for these changes instead of policing; scheduling frequent visits to provide timely feedback; considering treatment as a long-term process (most overweight develops over years and may require years to treat); and using proven behavioral change strategies, self-monitoring, achievable but challenging short-term and long-term goals, feedback, and contracting and rewards to encourage achieving these goals. Parental skills training can also be effective. Parents are taught to be contingent and consistent and to avoid giving mixed messages and reinforcing undesired behaviors. They are also taught to be observant of their children's behaviors so they can reward them when appropriate, to direct their praise at children's behaviors instead of their personal attributes, to model desired behaviors, to deal with setbacks, to have patience for changes in behavior, and to set limits—saying "no" when necessary.[9]

All excess weight, regardless of the underlying cause, results from excess calorie consumption over calorie expenditure. Therefore, the key element of any behavioral treatment boils down to sustained changes in diet, activity, or both. The most successful goals for diet and activity change are simple and explicit. For example, "eat fewer high-fat foods" and "do more exercise" are not useful behavioral goals compared with "switch from whole milk to fat-free milk," "replace soft drinks and juice drinks with water," "remove cookies and cakes from the home," "walk to school instead of driving at least 3 days per week," or "limit television viewing to 1 hour per day." A brief diet-and-activity history can elicit appropriate behaviors to target, and simple and explicit goals are necessary for self-monitoring, feedback, and rewards.

To complement the treatment of children who are already overweight, primary care physicians also can promote primary prevention. Little research has been done on obesity prevention in clinical settings, but the same behavioral techniques used in treatment apply. Children with an overweight parent should be especially targeted, although a calorie-balanced diet and increased physical activity are appropriate for almost all children and families, regardless of their risk for obesity.

Substantial attention has gone into public health approaches to prevention. These are community programs

that target all children. Because of the number of people involved, small improvements in the population as a whole can produce even greater reductions in morbidity and mortality than effective treatment interventions involving only high-risk patients. Like treatments, however, these public health interventions are not always successful. Traditional school and community health education approaches have produced few benefits in body weight, but a handful of behaviorally based programs have proved successful. Examples include a school-based self-directed behavior change program for adolescents[10]; substituting popular dance or vigorous endurance training for regular physical education for middle-school students[11,12]; and a curriculum to reduce television, videotape, and video game use in elementary school children.[13] If more successful programs like these can be developed and disseminated, population-based prevention may hold the greatest promise for addressing the epidemic of pediatric obesity. Primary care providers can be effective advocates for the adoption of evidence-based public health programs in their local schools and communities, while also providing counseling and therapy for their overweight patients and families.

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Direct-to-consumer advertising of prescription drugs

These ads present both perils and opportunities

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The pharmaceutical industry has long relied on marketing to move drugs from manufacturers' laboratories to consumers' medicine cabinets. From 1938, with the passage of the Food, Drug and Cosmetic Act, until the mid-1980s, the industry focused its efforts almost entirely on physicians. Correctly recognizing physicians as their principal customer, drug manufacturers deployed large armies of sales representatives who marched into physicians' offices bearing promotional materials, drug samples, coffee mugs, "continuing education" dinner invitations, and baseball tickets.

Relying solely on promotion to physicians made sense when they exercised uncontested control over prescribing, but changing times have meant changing strategies. In recent years, the phenomenon known generically as "managed care" has sparked the widespread proliferation of drug formularies, utilization review systems, and pharmaceutical risk-sharing agreements. As a result, physicians cannot just prescribe whatever seems reasonable and appropriate following a delicious drug company–sponsored scampi dinner. They must sometimes be pushed to prescribe and to insist—in the face of resistance from group medical directors and chairs of formulary committees—on the brand name drug over the generic, the new drug over the old, and the profitable drug over the unprofitable. And who better to provide the pushing than the patient, now an enlightened "health care consumer"?

Drawing on these insights, the pharmaceutical industry has altered its marketing strategy to include direct-to-consumer advertising. The Food and Drug Administra-

tion, after a long moratorium, decided that these ads required no new regulation beyond the "fair balance provision" of the 1962 Kefauver-Harris amendments, which requires that manufacturers truthfully present a fair balance of risks—side effects and contraindications—and effectiveness. Expenditure for this advertising currently comprises 15% to 20% of total drug marketing costs and is projected to increase to $7.5 billion by 2005.

The arguments for and against direct-to-consumer advertising are already becoming a little tiresome, even to one who has been actively engaged in the debate.[1,2] In general, proponents claim that "by greatly increasing the likelihood that patients will seek help for their medical problems and receive a safe and effective prescribed medicine, DTC advertising will . . . play a very real role in enhancing public health."[3]

Critics counter that

> extending the scope of already ubiquitous promotions about "post-nasal drip," "unsightly rashes," or "cures" for baldness has little to do with educating patients or relieving suffering. It will, however, inevitably drain healthcare dollars, dramatically increase unnecessary prescribing, and strain patient-doctor relationships.[4]

With nothing less than the health of the public at stake, not to mention billions of dollars, it is no wonder that the debate has veered toward acrimony. Each side has tended to overstate its case. Yes, these ads may prompt some patients to seek care for previously undiagnosed and untreated conditions. And, yes, they may spur other patients to make unnecessary visits to the doctor and to incur the risk of medication side effects while gaining little benefit. However, the net benefits and risks of direct-to-consumer promotion are unknown. The research required to make these assessments is difficult.

Drug manufacturers should do more educating and less selling

The net public health gain or loss of this advertising will be determined by 3 things: the current prevalence of undertreatment (the number of patients not receiving drug therapy who should be), the amount of inappropriate or harmful prescribing that might be stimulated by such ads, and the degree of harm accruing to undertreated compared with overtreated patients. Until substantial resources are allocated to this research agenda, we will not know which side is right. In practical terms, however, it may not matter. Direct-to-consumer advertising is here to stay. The real question is how it should be delivered so as to maximize the benefits while minimizing potential harms.

Here is my prescription. Drug manufacturers should do more educating and less selling. This means focusing on conditions rather than drugs; assisting patients with home-based triage and self-care; presenting information on treatment alternatives, including nonpharmacologic therapies; helping patients who decide on medication to optimize adherence; and promoting partnerships with physicians. As an example of partnership, drug firms should alert physicians before launching direct-to-consumer ad campaigns and help them prepare for questions their patients are likely to ask. Government should, in the words of an American College of Physicians' position paper, "impose serious limits on the pharmaceutical industry to ensure that consumers receive complete and nonconfusing information."[5] The FDA's current policy of retrospective review is inadequate. Government should also fund research to ensure that in 5 years we will know more about the true benefits and risks of this advertising. The medical profession should partner with government, foundations, and the news media to create sources of objective consumer drug information, such as a "Medical Letter" to consumers, and public service announcements alerting consumers of undertreated conditions, like depression and hyperlipidemia. In the meantime, physicians should brace themselves for growing hordes of patients bearing ads.

The true net benefits and risks of direct-to-consumer promotion are unknown

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Guidelines for managing acute bacterial meningitis in adults

Speed in diagnosis and treatment is essential

Nearly 1 in 4 adults with acute bacterial meningitis die, and many survivors sustain neurologic deficits.[1,2] The outcome has not changed since the early 1960s despite the introduction of potent antibiotics and specialized intensive care units.[3] Can anything further be done to optimize treatment and improve outcome?

The prognosis is worse with a delay in management.[4] Consequently, the outcome depends on whether the attending physician suspects acute bacterial meningitis and whether the health care system is set up to make a rapid, accurate diagnosis and initiate fast and effective treatment.

In this respect, standardized guidelines such as those recently issued by the working party of the British Infection Society are invaluable.[5] These guidelines make recommendations for the management of adults with suspected or diagnosed acute bacterial meningitis or meningococcal disease and for the prevention of secondary cases by vaccination and prophylactic antibiotic treatment. The guidelines may provide a template for treating acute bacterial meningitis for physicians in most countries. However, countries that now vaccinate against *Haemophilus influenzae* type b or meningococci serogroup C may see a change in the epidemiologic characteristics of bacterial meningitis.

There is little evidence on the best way to manage patients as soon as they present with acute bacterial meningitis. The new report advises family physicians to give benzylpenicillin (penicillin G) to any patients who may have acute bacterial meningitis before they are admitted to the hospital. With elderly patients, however, more caution may be needed. First, the outcome from acute bacterial meningitis has not been shown to be improved by the preadmission use of antibiotics; the crucial factor is probably whether the attending physician suspects acute bacterial meningitis at all and therefore arranges immediate admission to a hospital. Second, preadmission antibiotic use may make it harder to get a definitive microbial diagnosis.

For a young patient with suspected meningococcal disease, the immediate use of antibiotics, followed by rapid admission to a hospital, may be the best course of action. In patients with suspected bacterial meningitis of other causes, arranging rapid transfer to a hospital, followed by speedy microbiologic testing and antibiotic treatment, may be more prudent. After admission to the hospital, the widely accepted empiric treatment is the administration of a third-generation cephalosporin, such as cefotaxime sodium or ceftriaxone sodium, with ampicillin if listerial meningitis cannot be ruled out. In patients with obvious meningococcal disease, penicillin is the drug of choice.

The reduced susceptibility of pneumococci to penicillin is an increasing problem in large parts of the world; this may often be overcome by increasing the amount and frequency of doses, but rifampicin (rifampin) may be useful for pneumococci that are truly penicillin-resistant.[6] Selecting the appropriate therapy for patients with acute bacterial meningitis who are hypersensitive to β lactams is difficult. Chloramphenicol is not ideal because of its low clinical efficacy and potential side effects; meropenem or broad-spectrum quinolones may be considered, although there is little evidence that they work.

Supportive treatment has been hotly debated. Corticosteroids reduce neurologic deficits in children with *H influenzae* meningitis, whereas their beneficial effect in adults remains to be proved.[7] It is hoped that the results of the multicenter European trial on dexamethasone use in acute bacterial meningitis, scheduled to end in a year, will provide conclusive evidence. The use of glycerol or mannitol may reduce intracranial pressure when there is intracranial hypertension.[8] The need for full fluid replacement and maintenance is rightfully emphasized in the guidelines. Fluid restriction does not lessen brain edema or improve outcome in patients with acute bacterial meningitis.[9,10] Furthermore, cerebral perfusion depends on the mean arterial blood pressure in these patients and is adversely affected by hypovolemia.[11] Also, these patients are at risk of sepsis with hypotension. In general, many patients with acute bacterial meningitis need intensive care to monitor and treat both cerebral and extracerebral complications.

The guidelines are the laudable result of a major effort from the working party and should be disseminated to all physicians. An increased awareness of acute bacterial meningitis with emphasis on speedy diagnosis and treatment will serve patients well.

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A book that made me think

Bioethics: An Anthology, Helga Kuhse, Peter Singer, eds. Blackwell Publishers, $39.95, pp 600, ISBN 0 631 20311 7

Peter Singer was a keynote speaker at the last annual meeting of the American Society of Bioethics and Humanities in Philadelphia. For various reasons, I had chosen this moment in the program to duck out of the conference. I was completely unprepared for what greeted me as I left the hotel—protesters, many confined to wheelchairs, chanting "Less debate, more hate." This, I discovered, was the disability activist group Not Dead Yet, which is incensed about Singer's stance that some people with disabilities are not "persons" and may be killed or allowed to die with impunity. It is rare for philosophers to incite the ire of the community at large. Socrates and Bertrand Russell did, and now it seems Peter Singer has joined the ranks of infamy.

I am disappointed by Kuhse and Singer's edited collection of philosophical papers on bioethics. The selection is deeply conservative, and it eschews literature at the margins of bioethics. This is a shame because contemplation of narrative ethics, anthropology, families, and communities is where the action has been in bioethics during the past decade. My attention was naturally drawn to the four essays by Singer himself in the volume. Here, I was not disappointed but offended. Singer variously concluded that experimenting on a human embryo is preferable to doing so on a mouse; that chimpanzees are properly called "people," but humans with profound cognitive impairments are not; and that the heart of a handicapped newborn human might be legitimately excised to save a baboon in need of a new heart. Some have argued that Singer is not responsible for these absurd conclusions since he is merely working through the logical outcomes of a particular moral theory, utilitarianism. Whatever faults we may find with the outcome are properly attributed to the theory and not the philosopher. I disagree: Singer is culpable for these views because doing ethics responsibly involves more than logical reasoning alone. Moral intuition acts as an important check on ethical reasoning, telling us that at times it is the theory, not our actions, that must be changed. More than once Singer notes, "At first this sounds crazy," and more than once he fails for not paying attention to his own intuition.

My reaction to Singer's work is akin to discovering that a friend has served me her pet for dinner. As my initial reaction of disgust fades, I would wonder whether the animal was really a pet, and, if it was, whether my friend actually understands what it means to have a pet. Having a pet implies a set of rules describing the proper relationship between owner and pet and not eating one's pet is high on the list. The terms "person" and "animal" come with their own sets of rules, embedded deep within our society, defining relationships among human beings and between people and animals. Singer, in suggesting that these terms or the rules associated with them may be interchangeable, demonstrates that he fails to understand the concepts of "person" and "animal" at all.

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This review first appeared in the *BMJ* 2000;320:1215

Point-Counterpoint

Should physicians be required to report domestic violence to the police?

For: Mandatory reporting is worthy of support

Carolyn J Sachs

Domestic violence injuries are "criminal acts" in every state and, as such, are covered under most assault reporting laws. Although domestic violence is only 1 type of assault that requires reporting, it is the only type that has drawn substantial opposition.

Admittedly, mandatory reporting of any condition conflicts with patients' rights to privacy. Those opposed also worry that injured patients may avoid seeking care out of fear of police involvement and that this involvement could anger a perpetrator to increased aggression. However, these concerns remain theoretic because we lack prospective data to corroborate them. Survey studies of both abused and nonabused patients in hospitals and shelters have found that a clear majority in each group supports mandatory reporting of domestic violence, and more than 87% would not be deterred from seeking medical care in the setting of mandatory reporting.[1,2]

Reporting laws can increase the detection and documentation of abuse, aid in appropriately referring victims, and ensure perpetrator investigation. Police reporting reinforces that domestic violence is a crime and may increase victim safety by providing immediate access to restraining orders and swift perpetrator arrest. Clearly, simply reporting any abusive act to police does not guarantee an effective solution to the problem. A coordinated response team that includes victims' advocates, educated medical personnel, and appropriate agency response is the cornerstone for the management of any abuse in the medical setting.

In any situation that involves heated controversy and little outcome data, we must decide the age-old question: Does the possible end justify the means? As a society, we have accepted the concept of mandatory reporting for child abuse, elder abuse, and assault victims because the ultimate safety of these groups is an end worth the means of mandatory reporting. If we accept mandatory reporting for these populations, we would do a disservice to domestic violence victims by excluding them from mandatory reporting. In essence, an injury to a man in a weekend beer brawl would require police reporting but not an injury to a woman attacked by her husband. The isolated exclusion of domestic violence from mandatory reporting reverts such incidents back to being characterized as a "family matter" not worthy of the protection afforded other victims of assault and abuse.

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Against: Mandatory reporting does not guarantee safety

Michael A Rodriguez

Mandating that health care providers report intimate partner abuse injuries to police, even against patients' wishes, may have 4 major deleterious consequences.

First, mandatory reporting may increase partner abuse victims' risk for retaliatory abuse. As many as 50% of abusers make such threats, and more than 30% assault their partners during prosecution,[1] illustrating the clear and present danger faced by intimate partner abuse victims whose abuse is reported to police.

Second, mandatory reporting may also deter victims of intimate partner abuse from seeking appropriate medical care. Wishing to avoid contact with police, some victims may not disclose the source of their injuries to their providers. Undocumented abused women fearing deportation and women who fear losing custody of their children are particularly vulnerable. This further isolates partner abuse victims and limits the ability of physicians to intervene on their behalf and provide the best possible care.

Third, mandatory reporting may create expectations of services and protection that cannot be met. Limited or unsafe police response to reports of intimate partner abuse may further endanger victims, undermine victims' trust in the criminal justice system, and hinder the system's efforts toward punishment and deterrence.

Finally, and perhaps most importantly, mandatory reporting may compromise patients' autonomy and the confidentiality of patient-physician relationships. Unlike mandatory reporting of child abuse, reporting of intimate partner abuse nearly always involves competent adults capable of making critical life decisions. It deprives victims of their right to decide whether and how to involve law enforcement agencies. It breaches patient-physician confidentiality and creates a barrier to the open and honest exchange required for proper diagnosis, treatment, and follow-up.

Clearly, mandatory reporting raises serious professional and ethical considerations for both patients and physicians.[2] However, its direct effects and possible risks have not yet been studied. In the absence of solid research to support it, its benefits must be questioned. Does mandatory reporting contribute to the greater safety and well-being of partner abuse survivors? Quite possibly it does not.

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In the Public Eye

News and Features

Women physicians earn $63,000 less than male counterparts

Deborah Josefson, San Francisco

Researchers at the University of Pittsburgh's Graduate School of Public Health have found a persistent sex bias in physicians' salaries, with women earning on average 14% less than their male counterparts (*Ann Intern Med* 2000;133:104-110).

The study, led by Dr Roberta Ness, focused predominantly on nonacademic physicians and surveyed 232 male and 213 female internists practicing in Pennsylvania. All had been out of medical school for 10 to 30 years, and 85% of the respondents were in their 40s and 50s.

The questionnaires completed by the physicians provided information on demographics; training; board certification; practice type and setting; hours worked per week; division of time between patient care, teaching, research, and administration; and faculty appointment and promotion. In addition, information on marital status, number and ages of children, and leave from work was assessed.

Specialties were divided into high-earning and low-earning categories. High-earning subspecialties included cardiology, hematology/oncology, gastroenterology, and pulmonary/critical care. Low earners encompassed allergy and immunology, geriatrics, infectious disease, endocrinology, rheumatology, nephrology, and general medicine.

Results of the survey showed that women physicians were more likely than men to be in low-paying specialties and to be salaried employees rather than partners or in private practice. In general, female physicians saw fewer patients and did less administrative work but spent as much time as the men teaching, doing paperwork related to patient care, and doing research.

Moreover, women physicians tended to have fewer children than their male counterparts but were more likely to have taken time off from work or to have worked part time. Among those women who took time off or reduced their working hours, 82% said it was for maternity leave or child care purposes; only 19% of men took time off for these reasons.

AP Photo/NBC, Danny Feld

Does Dr Weaver earn less?

Even after adjusting for differences in compensation among various medical specialties and for hours worked per week, the investigators found a salary inequality, with women earning 14% less an hour than male counterparts.

Left unadjusted, the gap is 28% per hour less. On average, men earn $63,000 a year more than women.

Commenting on the results of the study, Dr Ness said: "Over the past 20 years, women have accounted for an increasing percentage of the US physician workforce, yet they have lagged behind their male colleagues in terms of career success. . . . Our results show that in terms of salary—perhaps the most important marker of gender equity at work—these women are behind men."

Previous research on differences between the sexes in physicians' salaries focused on academics and showed similar findings. Three quarters of the respondents in this survey were nonacademic physicians.

Global News Roundup

Gene therapy can shrink tumors

A trial involving 30 patients with recurrent head and neck cancer found that those who received gene therapy plus chemotherapy had more tumor regression than those receiving chemotherapy alone. For most of these patients, surgery or radiotherapy had already failed. Researchers used a virus to deliver therapeutic genes to sites of recurrent cancer. In 19 patients, the tumors shrank by 50% or more, and in 8 of these, the tumors disappeared (*Nat Med* 2000;8:879-885). A phase 3 trial is now under way.

Biodegradable stents developed

Japanese researchers have successfully tested biodegradable coronary artery stents, which may soon supersede metallic ones for coronary artery angioplasty. The stents are designed to be stable for at least 6 months and to disappear within 2 years. They may become useful as devices to deliver drugs such as heparin or platelet inhibitors. It is hoped that the stents will be less thrombogenic than metallic ones.

Interleukin boosts CD4 counts in people with HIV infection

Adding interleukin 2 to antiretroviral drug therapy substantially increases the CD4 cell count and decreases the viral load of HIV, according to a multicenter trial sponsored by the National Institutes of Health (*JAMA* 2000; 284:183-189). In the 2-year study, 82 patients were randomly allocated to receive antiretroviral drugs alone or drugs plus intermittent subcutaneous interleukin. There was a dose-related increase in CD4 counts in those treated with interleukin. Whether these results will translate into long-term clinical gains is still unclear.

Israeli surgeons implant first artificial ventricle

A terminally ill patient in Israel received the first artificial left ventricle, which functioned for several days before the man's death 5 days later from multiple organ failure. Dr Jacob Lavee, who performed the operation, said that the man would have died "within 6 hours" if he had not received the implant. The device, designed and manufactured in the United States, was inserted into his abdomen and was powered by a lithium battery outside his body. Most patients who need heart transplants have only a diseased left ventricle, so the new procedure may supersede heart transplantation.

Elizabeth Hurley sucks to stop smoking

Ron Davis, *BMJ*

During a recent photography shoot for a cosmetics advertisement on the Caribbean island of St Bartholomew, actress and model Elizabeth Hurley was caught by paparazzi sunbathing topless while sucking on a baby's pink pacifier [see www.bmj.com/cgi/content/full/321/7257/319/b].

British tabloid newspapers struggled to account for the actress's bizarre accessory. The *Mirror* explained that "there are few better ways to protect luscious lips from cracking or burning in harsh summer sun." Another tabloid surmised that Ms Hurley was not touched enough as a child and was continually regressing into an infantile state.

Finally, it came out that the pacifier was Ms Hurley's latest method to give up the half a pack of Marlboro Lights she smokes each day. A spokeswoman for Ms Hurley explained that nicotine patches did not seem to work for her. The idea for the pacifier, she said, came from Desmond Morris's book *Manwatching*, which "equated smoking with a baby's desire to be breast-fed."

Mr Morris was pleased to hear that Ms Hurley had taken his advice: "Only someone like Liz, whom I've never met, could make something like a dummy [pacifier] look chic and trendy. As far as I know, she's the only person to have taken up my idea to suck on a dummy to fight the urge to light up."

Actor Hugh Grant, Ms Hurley's former boyfriend, confirmed that she was an addicted smoker. "Elizabeth smokes 4,000 cigarettes a day. I've caught her with cigarettes in her nostrils," he told *Esquire* magazine last September.

Confirming her addiction to cigarettes, a web site devoted to female smoking celebrities lists 50 instances when the supermodel's smoking—or attempts to stop—have been shown or mentioned in newspapers, magazines, or movies (www.cs.brown.edu/~lsh/asfs/H/Hurley.html).

If the idea of sucking a pacifier to give up catches on, a randomized trial to measure its effectiveness may follow. Investigators may have difficulty, though, devising an appropriate placebo for the control condition.

Lumpectomy as good as mastectomy for tumors up to 5 cm across

Scott Gottlieb, New York

In women with breast cancers up to 5 cm across, the rates of long-term survival and metastasis-free survival are similar for mastectomy and breast-conserving treatment, according to a new study.

Previous studies have shown both approaches to be similar for women with tumors 2 cm or less across, for which breast-conserving treatment is widely used. But this is the first study to show equally good long-term results even when the width of a tumor is as much as 5 cm.

The results suggest that breast-conserving treatments, instead of mastectomy, could now be offered to most women with breast cancer, according to the researchers (*J Natl Cancer Inst* 2000;92:1143-1150).

Women who have tumors less than 2 cm across often undergo lumpectomy. For women with larger tumors, however, there was previously little evidence that breast-conserving surgery offered long-term benefits, according to the team of researchers led by Dr Harry Bartelink of the Netherlands Cancer Institute in Amsterdam. For these women, the recommended treatment is often modified radical mastectomy.

In the new study, researchers compared the survival of 868 women who were randomly assigned to undergo either lumpecto-

my or modified radical mastectomy to see whether women with tumors as wide as 5 cm could be treated effectively with breast-conserving surgery. Of these women, 696 had a tumor that measured 2.1 to 5 cm.

Ten years after surgery, no significant difference in survival was found in women with larger tumors, regardless of the type of surgery. Almost two thirds of the women in each group were still alive after 10 years. In addition, the cancer was no more likely to metastasize in women who had had a lumpectomy than in women who had had a mastectomy.

"This international trial has now shown that breast-conserving therapy results in a similar survival rate as mastectomy, even for patients with larger tumors," Dr Bartelink said. "Breast-conserving therapy instead of mastectomy can, therefore, now be offered to the large majority of the breast cancer population as the majority of patients in the western world nowadays present with tumors smaller than 5 cm."

Researchers, however, did find that about 20% of women in the lumpectomy group had a recurrence within 10 years, compared with about 12% in the mastectomy group, even if the recurrence did not affect 10-year survival. Researchers said that it was important for further studies to establish which subgroup of women is at greatest risk of recurrence.

$1 Billion drug deal creates debt for "tomorrow's AIDS orphans"

Annabel Ferriman, *BMJ*

The United States has offered sub-Saharan African nations a $1 billion loan program to buy anti-AIDS drugs. The new program was announced in Washington, DC, last week by the congressionally funded US Export-Import Bank. It involves 5-year loans to 24 eligible countries at interest rates of about 7% a year.

The offer has been condemned by Oxfam as "a debt that tomorrow's AIDS orphans will be forced to pay."

The US offer requires countries to buy drugs manufactured in the United States. Oxfam said that the loan would simply load more debt on countries that were already among the poorest in the world. "The deal amounts to a credit-line which locks poor countries into buying expensive patented drugs, when what they need is help to make or buy low-cost generic equivalents," Oxfam said in a press release.

It continued: "The G8 nations promised last year to write off $100 billion worth of poor country debt. But little of that has been delivered. For the US this week to offer these same poor countries another $1 billion of debt is wrong-headed." The debt owed by sub-Saharan African nations currently stands at $15.2 billion.

"This offer has been publicized as an act of kindness toward Africa's 24.5 million sufferers of HIV and AIDS. In fact, the money will flow straight into the pockets of the US pharmaceutical industry," said an Oxfam spokesperson.

Oxfam accused the United States of setting up the deal to help the drug companies fight off competition from generic drugs that can be manufactured locally. Brazil and India, for example, currently manufacture anti-AIDS drugs at a fraction of the cost of those marketed by multinational pharmaceutical companies.

The companies consider these generic drugs to be a violation of intellectual property that the companies say is protected by patents and trade agreements enforced by the World Trade Organization.

The anti-AIDS drug stavudine, for example, costs $6.10 per daily dose in Uganda, where it is marketed by Bristol-Myers Squibb, but just 55 cents in Brazil, where it is produced generically. Brazil and India are among the few countries in the world that started local production of anti-AIDS drugs before the World Trade Organization's rules on intellectual property rights were applied.

"The best way to begin helping the poor countries of sub-Saharan Africa is to cancel their debt so they can invest in health, education, and development," an Oxfam spokesman said.

capsule

Islet cell transplantation may be feasible President Clinton has named 6 centers that will participate in a trial in which 40 people with type 1 diabetes mellitus will receive islet cell transplants. In a recent case series, 7 diabetic patients had normal glycosylated hemoglobin levels for a median of 11.9 months after islet cell transplantation. The progress of the technique is likely to be impeded by the shortage of donor pancreases, the primary source of islets.

Media Watch

SAMe targets consumers via the Web

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Touted as one of the most promising supplements ever introduced, *S*-adenosyl-L-methionine, or SAMe (pronounced "Sammy"), is found advertised on the Internet, in health and drug stores, and even in direct-to-consumer television ads since its introduction in the United States last year. Discovered in the 1950s, SAMe has been used widely in Europe for a variety of maladies, including depression, osteoarthritis, and liver disorders. This dietary supplement has been sought by US consumers primarily for its mood-enhancing effects.

> Trials testing parenteral doses have shown SAMe to be effective for clinical depression

SAMe is a natural compound endogenously produced from adenosine triphosphate and the amino acid methionine. It then becomes a ubiquitous methyl donor to a wide variety of acceptor molecules and is involved in numerous metabolic pathways.[1] The exact mechanisms of action of SAMe for its purported health applications, principally as treatment of depression, are unknown. Limited animal and human data suggest that SAMe may play a role in alleviating depression by mechanisms such as modulating the monoaminergic systems and enhancing the neurotransmission resulting from the increase in neuronal membrane fluidity when modified by SAMe supplementation. The proposed neuropharmacologic effects of SAMe on depression have been extensively reviewed by several authors.[1-3]

Most early studies evaluating SAMe for depression were generally small and varied greatly in the patient population. A meta-analysis of selected clinical trials conducted for depression between 1973 and 1992 attempted to pool available data to assess the efficacy of SAMe compared with placebo (6 trials) and standard tricyclic antidepressants (7 trials). This study concluded that SAMe was more effective than placebo and comparably as effective as low to moderate dosages of tricyclic antidepressants.[4] However, the substantial heterogeneity among these individual trials—patient populations, sample sizes, variable dosage regimens, and treatment durations—may limit the results found in this analysis. More recently, additional small double-blind trials have yielded positive results.[5,6] Overall, trials testing parenteral doses have shown SAMe to be effective for clinical depression. Most trials have found the antidepressant effect to appear fairly rapidly (sometimes within 1 week) after the start of treatment. However, given the lack of large controlled trials and SAMe's questionable oral bioavailability, more data are needed to support its use orally.

SAMe may be administered orally, intravenously, or intramuscularly, but only the oral formulation is commercially available in the United States. Most controlled studies of oral SAMe have employed a daily divided dose of 1,600 mg—but marketed supplements often recommend lower doses. Besides mild gastrointestinal distress, SAMe is generally well tolerated and does not appear to possess cardiac, anticholinergic, or orthostatic effects that may limit the clinical utility of many prescriptive antidepressants.[7,8] Agitation and manic reactions have been reported to appear soon after SAMe administration.[9-12] For this reason, its use should be avoided in patients with a history of mania or bipolar disorders. There are no known confirmed drug interactions with SAMe. One case of serotonin syndrome in an elderly woman taking SAMe (intramuscularly) concurrently with clomipramine hydrochloride has been documented.[13] The safety of concurrent use with the commonly prescribed selective serotonin reuptake inhibitors has not been evaluated. The coadministration of SAMe (intramuscularly) with imipramine hydrochloride (to hasten the onset of response to imipramine) did not reveal significant adverse effects.[6]

> More data are needed to support its use orally

Consumers should be aware that the nutritional supplement industry is not well regulated and that the question of purity and potency remain. For instance, a company that conducts independent analyses of herbal, vitamin, and mineral supplements recently found disturbing discrepancies between the labeled amount and the actual amount of SAMe contained in various brand products selected for testing. Nearly half of the products evaluated did not pass testing.[14] Consumers and clinicians should also consider the cost of therapy. The monthly cost of SAMe,

depending on the dose used, may be well over $200, exceeding that of most prescription antidepressants.

The antidepressant potential of SAMe has generated much enthusiasm in this country lately, especially through the lay press. However, its claims of efficacy and safety for the treatment of depression need to be further justified through large controlled trials and by formal evaluation by the Food and Drug Administration. Follow-up studies to assess long-term tolerability and relapse rates are also needed.

At the time of this writing, Linda Shu was a 4th-year pharmacy student at the University of California, San Francisco, School of Pharmacy.

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PR News Photo/American Lung Association

Slides such as this one have appeared before feature films in some theatres in California. Sponsors hope young viewers get the message, which is designed to respond to the portrayal of tobacco use in movies as stylish and cool.

Med. Pix

What is in a name?

QUESTION: A 28-year-old African American man is concerned about a rash that he has had on his body on and off for many years. He denies any pain or itching in association with the rash, although it is more pronounced in the summer months and when he is sweating. The patient is otherwise well. He states that he is in a monogamous heterosexual relationship and practices safe sex.

Physical examination reveals hypopigmented macules on the chest, upper arms, and back, some of which have coalesced into larger hypopigmented areas. Close visual inspection shows that there is a light scale over the macules. There are no lesions in the mouth or on the hands, feet, or genitals.

What is the differential diagnosis, and what further tests would help you make the diagnosis?

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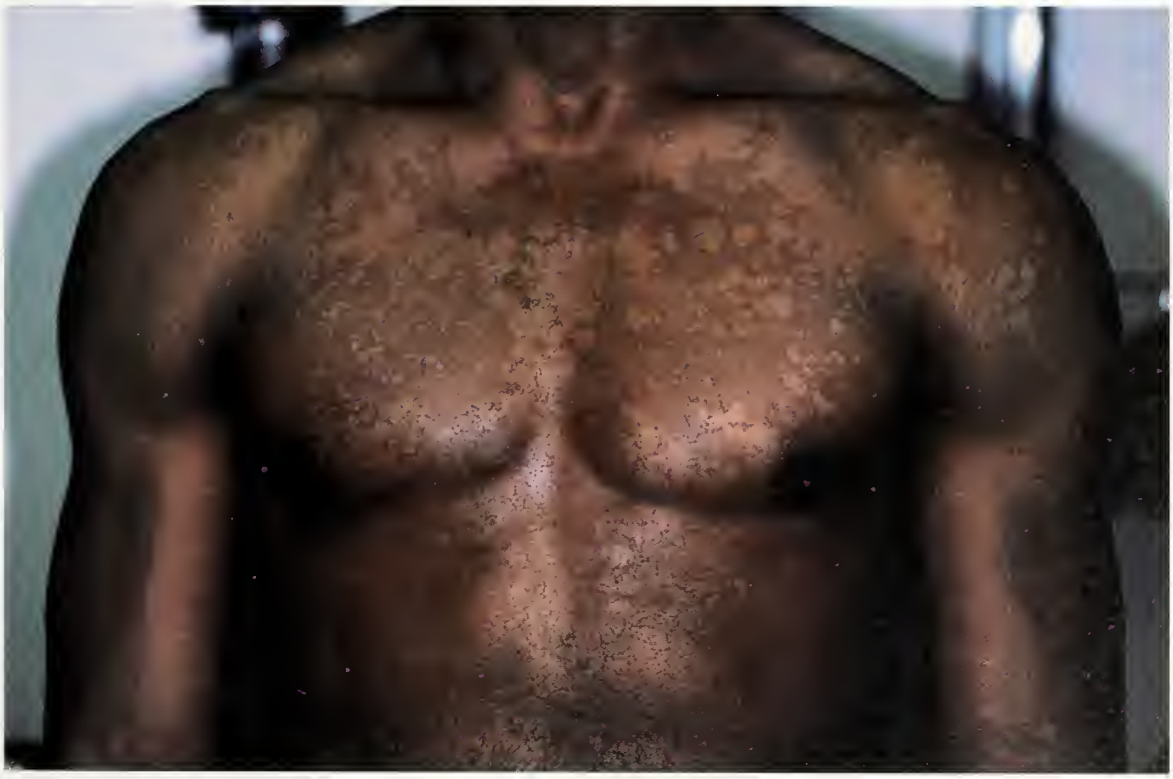

ANSWER: The differential diagnosis includes tinea versicolor, vitiligo, pityriasis rosea, and secondary syphilis. With the use of a microscope slide, scale from the macules was scraped to a second slide. Potassium hydroxide (KOH) with dimethyl sulfoxide was placed on this slide and covered with a coverslip. Microscopic examination revealed the typical "spaghetti and meatballs" pattern of tinea versicolor. The spaghetti represents broken hyphae and the meatballs are the spores of *Pityrosporum ovale*.

DISTRIBUTION AND TERMINOLOGY

Pityrosporum ovale, the same organism as *P orbiculare*, may be seen in association with *Pityrosporum* folliculitis, seborrhea, and tinea versicolor. *Pityrosporum* organisms thrive in moisture and tend to grow on the skin in areas where sebaceous follicles secrete sebum. Tinea versicolor is found on the chest, upper arms, and back. Seborrhea tends to manifest on the scalp, face, and chest.

Tinea versicolor is also called pityriasis versicolor, a name that makes reference to the connection between this condition and the *Pityrosporum* species. Tinea versicolor is more closely related to seborrhea than to tinea corporis, which explains why tinea versicolor responds to therapeutic agents used to treat seborrhea and dandruff and does not respond to medicines such as griseofulvin that are used to treat tinea corporis and tinea capitis.

DIFFERENTIAL DIAGNOSIS

Vitiligo causes full depigmentation of the skin, which is distinct from the hypopigmentation that is associated with tinea versicolor. The lesions of pityriasis rosea have a fine collarette scale around their border, and a herald patch is frequently seen. Scaling usually is not a characteristic of secondary syphilis, which is more commonly associated with macules on the palms and soles. In none of these conditions are hyphae and spores visible on KOH-treated scraping samples. When results of KOH specimen analysis are inconclusive and secondary syphilis is suspected, a VDRL test is recommended.

TREATMENT

Treatment of tinea versicolor is mostly for cosmetic reasons; patients usually are asymptomatic. The mainstay of treatment is topical therapy using antidandruff shampoos. Selenium sulfide 2.5% lotion or shampoo or zinc pyrithione may be applied to the involved areas daily for 1 to 2 weeks. A typical regimen involves applying the lotion or shampoo to the involved areas for 10 to 15 minutes and then washing it off in the shower. Another method involves applying the lotion for 24 hours before washing it off. Ketoconazole 2% shampoo, used as a single application or daily for 3 days, is also safe and effective treatment.[1]

Topical antifungal creams are expensive, particularly if they are applied over large areas. For smaller areas of involvement, the topical antifungal creams that work best include ketoconazole and clotrimazole.

A single oral dose of ketoconazole (400 mg) is a more convenient method of treatment than is applying a topical preparation daily for 1 to 2 weeks. Physicians should question patients about possible preexisting liver disease and warn them about the risk of liver toxicity with its use. Although the risk of liver toxicity with a single oral dose of ketoconazole is small, it is best to remember that most often the treatment is for cosmetic reasons.

The first sign of successful treatment is the lack of scale. Sun exposure hastens the normalization of skin color.

OUTCOME

The patient did not have health insurance coverage and so chose to use an over-the-counter dandruff shampoo for treatment and to seek additional care as needed. He was told he could repeat this treatment periodically to prevent recurrence of tinea versicolor. The patient has not been seen again for this condition.

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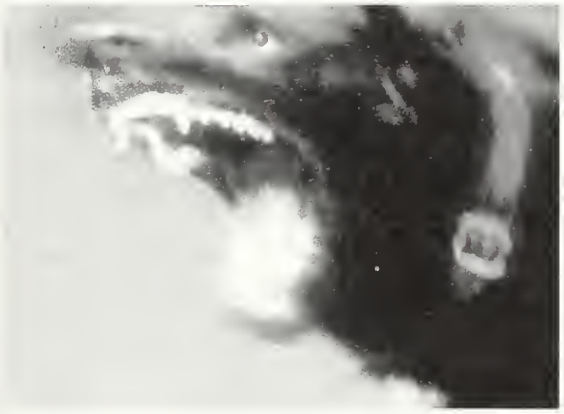
Original Research

Preventing dog bites in children: randomized controlled trial of an educational intervention

Dog bites are a major cause of injury, particularly in children.[1,2] Guidelines on prevention are generally unevaluated and include controlling high-risk breeds, keeping dogs on a leash, animal training, and educating dog owners.[3,4] However, no evaluations have been done of interventions designed to teach people how to avoid being attacked by a dog.

"Prevent-a-Bite" is an educational program designed for primary school children.[5] The program aims to instil precautionary behavior around dogs, assuming that this might reduce the incidence of attacks. A randomized controlled trial of the efficacy of the intervention was conducted in Australian children aged 7 to 8 years who were presented with an unsupervised opportunity to approach a strange dog.



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PARTICIPANTS, METHODS, AND RESULTS

Eight primary schools in metropolitan Sydney were randomly selected to participate in the trial, and all agreed to do so. The schools were cluster randomized into intervention and nonintervention control schools (4 in each group), and 2 classes in each school were then selected to participate. Altogether, 346 children aged 7 to 8 years took part. The study was approved by the human ethics committee of the University of Sydney.

The intervention consisted of a 30-minute lesson conducted by an accredited dog handler. The handler and dog demonstrated various "do's" and "don'ts" of behavior around dogs, such as how to recognize friendly, angry, or frightened dogs and how children should approach dogs and owners when they wanted to pat a dog. Children practiced petting the dog in the correct manner—asking permission, approaching slowly, extending the hand palm down, petting the dog under the chin and on the chest, avoiding eye contact, and walking away slowly and quietly—and precautionary and protective body posture to adopt when approached or knocked over by a dog. They were also told when not to disturb even a friendly, known dog (for example, when it is sleeping, eating, tied up, or in a car). A resource kit for teachers, which included activities to be undertaken before and after the demonstration, was also distributed.

Seven to 10 days after participating in the program, children in the intervention schools were allowed to play unsupervised in the school grounds. A docile Labrador dog was tethered 5 m (about 16 ft) away from its owner, who was disguised as a tradesperson. The children were not told that the dog was there and were videotaped by a hidden camera for 10 minutes. Children in control schools who had not received the intervention were let out to play in similar circumstances.

The number of children who breached the proscribed behaviors was tallied from the videotape by 3 of us, 1 of whom was blind to the intervention or control status of each school. When the 3 reviewers differed in their scoring of whether an approach to the dog should be recorded as a breach of the guidelines, the videotape was reconsidered and the behavior scored as a breach only if all observers agreed.

Children who had received the intervention displayed appreciably greater precautionary behavior than children in the control schools (table). They were circumspect, typically observing the dog from a distance. Most of the

Petting of dogs in intervention and control schools

School	No. of children	No. (%) who petted
Control		
1 (mixed)	37	19 (51)
2 (girls)	31	19 (61)
3 (boys)	42	41 (98)
4 (boys)	39	39 (100)
Total	149	118 (79)
Intervention		
5 (mixed)	47	8 (17)
6 (mixed)	55	1 (2)
7 (mixed)	36	2 (6)
8 (mixed)	59	7 (12)
Total	197	18 (9)*

*$\chi^2_1 = 212.30$; $P > 0.001$ for intervention versus control schools.

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Competing interests: J C, J R, and L S are paid consultants to the Delta Society of Australia. S C has been paid an honorarium and travel expenses for speaking at a meeting about the intervention.

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children in the control group (118 [79%] of 149) petted the dog without hesitation and tried to excite it, but only a few (18 [9%] of 197) of the children who had received the intervention petted the dog, and they did this surreptitiously or only after a considerable period of careful assessment.

COMMENT

The Prevent-a-Bite educational intervention increased appreciably the precautionary behavior of young children around strange dogs in the short term. Further research is needed to determine whether the program is able to influence children's behavior in the longer term, whether "booster" interventions can help sustain this behavior, observations in contexts outside school would show a similar magnitude of effect, and wide adoption of the program would reduce the number of children bitten by dogs.

S C designed the study, analyzed the video record, wrote the first draft, and is guarantor. J C convened the group who planned and conducted the trial and contributed comments on the paper. J R conducted the intervention, analyzed the video record, and helped write the paper. L S organized school participation, analyzed the video record, and helped write the paper.

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COMMENTARY

Bark, don't bite!

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Competing interests:
None declared

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Dog-bite injuries to children are more than a nuisance. There are about 334,000 emergency department visits and 20 deaths from dog-bite injuries each year in the United States, and the highest incidence is in children—especially boys aged 5 to 9 years. Children seen in emergency departments are more likely than older persons (73% vs 30%) to be bitten on the face, neck, and head.[1,2] Severe dog bites can lead to devastating injuries and death. Unfortunately, there is a paucity of analytic epidemiologic data to guide our prevention strategies.[3]

This is the first randomized controlled trial of a primary prevention intervention to reduce the prevalence of these injuries. As in most public health and injury interventions, tackling the dog-bite problem would logically start with attempts to control the environment, the agent (the dog), or both. These could include physical measures to separate children from strange dogs, restricting sales and ownership of high-risk breeds, and enforcing leash laws. The study by Chapman and colleagues is aimed at the host (the child) and uses a relatively short classroom curriculum to teach children appropriate techniques for approaching dogs.

The study is a refreshing move beyond describing the problem and its consequences. The authors used a cluster randomized trial design and relied on observational measures of how children actually approach a strange, tethered dog at school. The results of this study are impressive. There was a 70% absolute reduction in the proportion of children who petted a strange dog without hesitation. The magnitude of this difference is unlikely to be due to confounding or baseline differences between groups, but more information on the comparability of the 2 groups would be helpful.

The impressive nature of these results leads to more questions, some of which the authors raise in their own discussion. Short-term interventions of any kind often lead to impressive results, but the effect may decay considerably over time. Also, did the presence of the handler affect the nature of the child-dog interaction, making the scenario less than realistic? The intervention appears to work if the child approaches a tethered dog, but what proportion of children who are bitten have been approached by a menacing, unleashed dog? Would these skills have had an effect in such an encounter? Finally, the outcome measure was only a proximate measure. We do not know if decreased petting behavior will translate to fewer bite injuries.

The authors deserve considerable credit for their efforts to evaluate a preventive effort to reduce the prevalence of dog-bite injuries. Let's hope that this initial effort will lead to further studies that show that a dog's bark will be worse than its bite.

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Grievances against physicians: 11 years' experience of a medical society grievance committee

ABSTRACT **Objective** To understand causes of patient dissatisfaction that result in complaints. **Design** Grievances received by the grievance committee between January 1, 1989, and January 1, 2000, were reviewed. **Setting** A 2-county area of North Carolina. **Subjects** Of 29 patients who filed grievances, the 9 male (31%) and 20 female (69%) patients had a mean (±SD) age of 39 (±19) years. In 18 instances, the patient consulted the physician less than 3 times (64%) before the complaint and in 8 instances more than 4 times (29%). **Main outcome measures** Allegations of the grievance and the committee's findings. **Results** Grievances fell into 5 categories: failure to fulfill expectations for examination and treatment (38%), failure to promptly diagnose (20%), rudeness (17%), producing excessive pain or practicing beyond the area of expertise (13%), and inappropriate behavior related to billings (10%). In 45% of the grievances, the committee found no breach of practice standards. In 17% of the cases, the physician resolved the grievance by apologizing, adjusting a bill, or completing insurance forms. **Conclusion** Most grievances were filed by younger women against newly encountered physicians and were related to inadequate communication or alleged delay in diagnosis.

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INTRODUCTION

Dissatisfied patients act in various ways. Some ignore their physician's advice, others seek a new physician, and assertive patients may confront their physician. It is common for patients to discuss their displeasure with friends and relatives.[1-3]

Patients whose dissatisfaction prompts formal action have several options. These include bringing a malpractice claim and seeking redress in the courts, filing a complaint with the state medical board, complaining to the "patient relations office" of a hospital or group practice, directing a complaint to the hospital's chief of medical staff or credentials office, or submitting a grievance to the medical society. Why some dissatisfied patients do nothing and others take formal action is not known. Studying formal complaints seems a reasonable way of increasing our understanding of how patient-physician interactions go awry.

Americans are accustomed to complaining. In business, consumers are invited to file complaints or "see the manager" when they are dissatisfied. Complaints may be expressed by writing to or phoning a customer relations department, the Better Business Bureau, a governmental office of consumer affairs, attorney generals' offices, or a television station's consumer action reporter. If clients are sufficiently angered by the performance of their attorney, they might elect to take the matter up with the American Bar Association. There is, similarly, a long-standing practice of patients filing complaints with medical societies when they feel that a physician's conduct is inappropriate. Medical societies have, in turn, established policies and procedures for responding to complaints about their members.[4-6] Part of the societal contract between the medical profession and the public is the agreement that the profession will respond to complaints and be self-policing.

We have reviewed the experience of a medical society grievance committee to gain a better understanding of the causes of patient dissatisfaction. We hope that the knowledge gained will help develop preventive strategies.

METHODS

Grievance process

Medical societies generally process complaints against physicians through a grievance committee (also called a conciliation committee) and a disciplinary committee. The grievance committee screens, reviews, and refers complaints. In addition, the committee educates physicians and their patients about the professional obligations of physicians and decides whether to pursue disciplinary proceedings. If a disciplinary proceeding is appropriate, then the matter is referred to the disciplinary committee. The independence of the 2 committees is intended to ensure that a judgment concerning discipline is rendered by an impartial decision maker.[5] Although most complaints are filed by patients, they may be also filed by family or friends of the patient or colleagues of the physician. Complaints are submitted in writing. When this is not feasible because of a patient's impairment, the complaint is presented orally with a verbatim transcript taken.

When a complaint is received, the patient is asked to sign a release of medical information so that the complaint

can be evaluated. The committee evaluates the medical records and interviews the complainant, the physician, and any other person who has knowledge of the facts involved. In some cases, other physicians in the defendant physician's specialty are interviewed, and the medical society records are examined for any previous complaints concerning the physician.

On completing the review, a committee may reach 1 of 5 possible conclusions. The first is that the physician did not act improperly, and no further proceedings are warranted. The second is that the matter should be referred to the disciplinary committee, state medical board, police, or another agency or institution for further proceedings. The third is that the physician acted inappropriately but not seriously enough to warrant disciplinary proceedings or proceedings by an outside agency. In some of these cases, a mutually agreed course of remediation may be undertaken. The final conclusion is that efforts will be made to resolve the matter through mediation. Grievance committees may entertain complaints about fees but cannot undertake any activity that constitutes price fixing.[4,5]

Population

There are 2,394 practicing physicians, not in training, in Durham and Orange counties, North Carolina. About 440 practicing physicians (18%), not including students or trainees, are members of the Durham-Orange County Medical Society, along with 129 retired physicians. The grievance committee is responsible for processing complaints concerning physicians practicing in the 2-county area.

RESULTS

From January 1, 1989, through January 1, 2000, 29 grievances were filed. The age range of the patients was 11 to 73 years (mean, 39±19 years; median, 36 years). There were 9 male (31%) and 20 female (69%) patients.

The medical specialties of the defendants in the grievance proceedings are shown in table 1. Of the 28 physician defendants, 10 (36%) were academicians and 18 (64%) in private practice. In 18 instances (64%), the patient had consulted the physician 3 times or less and, in 8 instances (29%), 4 times or more. In 2 cases, the number could not be determined.

As shown in table 2, the principal grievances fell into 5 categories: failure to fulfill expectations for examination and treatment, failure to make a prompt diagnosis, discourteous behavior, unacceptable medical practice, and issues related to billing and collections.

In 13 cases (45%), the committee found no breech of the standards of medical practice. In 5 cases (17%), the physician defendant apologized, adjusted a bill, or complied with a request to complete insurance or disability forms. One fifth of the grievances were terminated by the patient refusing to provide a written signed complaint or by a lack of jurisdiction of the committee (table 3).

Table 1 *Specialties of the 29 defendants in the grievance proceedings*

Specialty	Physicians, no. (%)
Internal medicine or its subspecialties	6 (21)
Emergency medicine	4 (14)
Dermatology	4 (14)
Orthopedic surgery	3 (10)
Obstetrics and gynecology	3 (10)
Family practice	2 (7)
Pediatrics	2 (7)
Ophthalmology	1 (3)
Plastic surgery	1 (3)
Neurosurgery	1 (3)
Neurology and urology	1 (3)*
Medically related corporation	1 (3)

*One of the complaints was against a neurologist and a urologist.

DISCUSSION

Principal findings

Most grievances were filed by younger women against newly encountered physicians. Most grievances were related to inadequate communication or alleged delay in diagnosis.

The 29 complaints received represent, for the most part, serious allegations. Some patients clearly depart from their physician's office feeling victimized or cheated.[6] Perhaps a clearer mutual understanding of the expectations for medical or surgical therapy would have avoided later dissatisfaction. Because women, on average, have more physician visits per year than men, it is not surprising that women constitute the majority of patients filing grievances.[7]

In some cases, the act of bringing a complaint leads to a resolution. When both parties to a dispute have to describe their roles in a disagreement to a third party, they often realize during the process of self-examination that they do not want to take the case further. Often people just want someone to listen to the cause of

Table 2 *Principal claims of the 29 grievances*

Complaint	No. (%)
Physician's alleged failure to fulfill the patient's expectations for examination and treatment	11 (38)
Inadequate outpatient therapy—"The doctor treated me, but I'm still in pain"	6
Failure to obtain informed consent for surgery	2
Inadequate physical examination	1
Lack of prompt attention following hospitalization	2
Alleged failure to make a prompt diagnosis	6 (20)
Cancer	3
Multiple sclerosis	1
Cardiovascular disease	1
Pilonidal cyst	1
Alleged rude or discourteous behavior	5 (17)
Rude	4
Failure to answer mail or return phone calls	1
Alleged unacceptable practice behavior	4 (13)
Producing excessive pain	3
Practicing outside area of expertise	1
Alleged inappropriate behavior related to billings and collections	3 (10)
Discharge from practice for nonpayment	1
Overbilling	1
Failure of 1 physician to pay another for locum tenens work	1

their unhappiness. Being given this opportunity may in itself be a satisfying outcome.[6] In our study, although in about half the cases the committee found no breach of the standards of medical practice, this does not always mean that they endorsed a physician's behavior. To our knowledge, no grievance brought before the committee was ever carried forward to litigation as a malpractice claim.

Weaknesses of the study

Our data are inadequate to address the question of whether certain physician specialties are more likely to be the subject of grievances. They cannot tell us whether complaints are made more commonly against academic or private practice physicians. Our study did not determine how many complaints were taken directly by patients to their physicians rather than being brought to the grievance committee. It is unclear whether the frequency of patient use of the medical society grievance procedure varies by geographic area, whether the nature of grievances is changing over time, and how grievances evaluated by our committee compare with those being dealt with by patient relations committees, ombudsmen, or medical staff offices. Some complaints, during the process of committing them to paper, seem less dramatic to patients than they initially thought, and they are dropped. It is also possible, of course, that some patients do not submit written complaints because of literacy problems or because, in their opinion, the grievance process "just isn't worth the effort."

Other studies

A study of complaints against Australian physicians showed that most concerned physician incompetence, practice outside the physician's capacity, the physician's use of alcohol or drugs, sexual misconduct, errors in prescribing, and insurance fraud.[8] In another study, Annandale and Hunt found that the most common causes of patient disagreements with physicians were diagnosis-related—that is, failure of the physician to make a diagnosis or a patient disagreement with the physician con-

Table 3 *Dispositions of 29 grievances by the grievance committee*

Disposition	Grievances, no. (%)
There was no breach of the standards of medical practice	13 (45)
The committee had no jurisdiction in the case	3 (10)
The plaintiff declined to provide a written, signed complaint	3 (10)
The committee was unable to make a determination concerning fault	2 (7)
The physician apologized to the patient	2 (7)
The physician completed the disability or insurance forms as requested	2 (7)
Case referred to the State Board of Medical Examiners	1 (3)
The physician adjusted the bill	1 (3)
The patient expressed gratitude "for being heard" and dropped the grievance	1 (3)
On the recommendation of the committee, the physician enrolled in a continuing medical education course	1 (3)

cerning a diagnosis, disagreements about a prescription, concerns related to the doctor-patient interaction, or alleged overtreatment or undertreatment.[1]

In 1980, Banov summarized grievances brought to a county medical society. These fell into 5 categories: disputes over fees, physician neglect or unavailability to the patient, misunderstanding or a breakdown in communication, improper treatment, or inappropriate physician conduct.[9] Banov saw more disputes over fees than our committee did. Twenty years ago, on our committee, fees were also commonly discussed. A physician in practice whose charges were thought to exceed customary community norms would be explicitly told to "lower his or her prices." Such issues have now been excluded from the agenda of grievance committees, lest they be accused of price fixing.[4,5]

In a study of complaints submitted in England and Wales in 1971, the most common were alleged inadequate or incorrect treatment, failure to visit or delaying visiting a patient, and failure to refer a patient for admission to a hospital or other specialist service.[3] In a study by Owen in England, the most common causes of complaints were alleged failure to diagnose or a delay in diagnosis (26%), failure to visit the patient in a timely manner (25%), and alleged error in prescribing (9%).[10] Levinson and associates have identified particular types of US physician-patient disagreements related to managed care. These include disputes over the allocation of health care resources (access to specialists, diagnostic tests, or treatments), disputes over access to care (access to the primary care physician and allotment of sufficient time for office visits), and disputes over financial arrangements (fees or disclosure of physician financial incentives).[11]

Klein reviewed the frequency of complaints sent to the National Health Service in England and compared them with estimates of the rates of patient dissatisfaction with physicians. Not surprisingly, formal complaints represented only the tip of the iceberg. Patients far more often deal with their dissatisfaction by complaining to family and friends or switching doctors than by submitting a written complaint.[3] The Harvard Medical Practice Study found that less than 2% of patients who had had adverse events caused by medical negligence filed malpractice claims. Clearly, medical malpractice claims represent only a small subset of adverse events.[12]

Meaning of the study

Disagreements between patients and their physician may cause patients to have diminished trust in the physician, be dissatisfied with clinical results, change their physician or health plan, file complaints, or seek litigation. For physicians, disagreements may result in frustration, anger, loss of control, and career dissatisfaction.[8]

Physicians should employ fundamental communication skills to avoid grievances: understand the patients' worries and concerns, express empathy, actively discuss care options, negotiate differences of opinion, and allow sufficient time for an adequate conversation.[11]

Physicians selected for membership of a grievance committee should command the respect of their peers. They should have a large reservoir of experience. Diplomacy, an understanding of human nature, and sound judgment are also crucial.[6]

Unanswered questions and future research

The challenge for physicians is to recognize patients' unfilled expectations and to engage patients in a discussion with the goal of identifying and ameliorating dissatisfaction while building a trusting therapeutic relationship.[11] Future research should focus on identifying and evaluating strategies to improve communication skills and minimize patient dissatisfaction.

Dr Stephen Lang reviewed the manuscript and made many helpful suggestions.

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COMMENTARY

Patient grievances are a continuing challenge for medical science

> "I want to believe that my physician is acting under higher moral principles and intellectual powers than a used-car dealer."[1]

This comment of a physician-patient nearing the end of an illustrious career summarizes a capitalist society's special expectations of physicians. Twenty years ago, those expectations were easier to meet. Today's physicians operate increasingly where ethics conflict with profits: less time to talk, research, and think and fewer incentives to care as well as cure. Diminished patient comfort, at least in the view of some, is acceptable as long as "outcomes" are not compromised. Halperin summarizes his 11 years of experience with a medical society's grievance committee in a well-known center of clinical practice in the country during this time of undiminished patient expectations and rapid change in the organization of medical care.

Denominators are often forgotten in the discussion of physician errors, malpractice suits, and aggrieved patients. Numerators—the bigger the better—make the news. Assuming that the 2,394 physicians practicing in Durham and Orange counties each experienced 2,000 patient encounters per year (10 per day) over these 11 years, there would be 53 million opportunities for patient discontent with care. Twenty-nine reported grievances produce a rate of 0.6 per 1,000,000. Overall, this record translates into a remarkable decade of amicable human interaction.

Low rates should not lead us to dismiss the problem of patient dissatisfaction. Just as we demonstrate great concern over airplane crashes, however infrequent, there is much to be said for zero tolerance for avoidable patient injury or fractured patient-physician relationships. Of more relevance, while we can count air mishaps or auto accidents easily, we cannot do the same for patient grievances. As Halperin reports, only a small fraction of patients injured as a result of medical negligence file a malpractice claim. In all likelihood, most patients go home angry but adjust and forget with time. Despite many attempts to collect and report data on adverse patient encounters, our knowledge of the scope and nature of the problem is limited by poor definitions and inadequate methods for data collection. Litigation might help to compensate some patients, but it thoroughly frustrates attempts to assess and study physician-patient disaffection. Even the National Practitioner Data Bank, the federal repository of disciplinary and malpractice actions against physicians, surely underreports patients' malpractice suits against their physicians.

Several recent reports have examined efforts to measure and improve relationships. Kraman and Hamm examined the Department of Veterans Affairs medical system's policy of full disclosure of medical mistakes to patients and their families, a policy implemented to maintain the physician's role as caregiver and advocate.[2] Such a radical departure from a posture of defense (or denial) must be accompanied by complete reporting and open discussion.[3] Hickson and colleagues document what we have long known: a physician's poor interpersonal skills can precipitate suits.[4] Their current research focuses on methods of identifying and counseling physicians at risk. Effective interventions are neither easy nor a priori worthwhile. A randomized controlled trial of a managed care continuing medical education program entitled "Thriving in a Busy Practice: Physician-Patient Communication" failed to demonstrate improved patient satisfaction in the intervention over the control group.[5] Reducing or settling grievances remains yet another in the long list of biomedical challenges that will not be solved with the mapping of the human genome.

Managed care, patients' rights, and patient access to care are political issues closely related to patient satisfaction. Halperin's report gives us yet another window on the nature of grievances. But reports about grievances are still too few. If every entity were able to collect and combine for analysis their data on such grievances, we might then begin to understand fully the nature of these disputes and, of more importance, to assess intelligently the effects of new laws and health care organizations on physician-patient relationships.

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Recruitment and retention in the Navajo Area Indian Health Service

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ABSTRACT **Objective** To determine why physicians and midlevel providers join, leave, or stay in Navajo Area Indian Health Service (IHS). **Design** Cross-sectional analysis of data obtained from questionnaires. **Setting** Navajo Area IHS hospitals. **Subjects** Navajo Area health care physicians and midlevel health care providers. **Main outcome measures** The prevalence of physicians and midlevel providers who plan to leave the Navajo Area IHS, the demographic characteristics of these physicians and midlevel providers, and the most common reasons for staying or leaving. **Results** A total of 221 (64%) physicians and midlevel providers responded. Of these, 58% planned to leave eventually, and 47% of all physicians and midlevel providers planned to leave in the next 3 years. Physicians and midlevel providers planning to leave tended to be younger than those planning to stay ($P = 0.009$). The most common reason to join the IHS was a desire to work in the Southwest, to stay was the quality of the medical staff, and to leave was lack of administrative support. **Conclusions** A high turnover rate of physicians and midlevel providers may occur in the next 3 years. A combination of factors specific to the provider, the institution, and the environment attracts physicians to the Navajo IHS and encourages them to stay. Factors that push physicians and midlevel providers to leave tend to be specific to the institution and are potentially amenable.

INTRODUCTION

The Indian Health Service (IHS), a division of the US Public Health Service, provides care to Native Americans, including the Navajo Nation. The IHS suffers from understaffing of physicians and midlevel health care providers; in 1998, an overall 16% vacancy rate existed for physicians.[1] Understaffing is a serious problem because it can restrict the range and quality of services provided.

In the past, efforts to correct this problem have focused on recruitment at the federal level. The Health Professions Support Team was formed to help coordinate recruitment activities at various service units, and a survey performed in 1998 questioned a random sample of IHS physicians as to what motivated them to join the IHS.[1] The Loan Repayment Program was designed to provide a financial incentive for physicians to join the IHS, and scholarship provides funds for medical school in return for a pledge to work in underserved areas. Title 38, federal legislation that allowed health service centers greater flexibility in setting pay scales, resulted in an increase in pay for many IHS physicians.

Although these efforts have probably assisted in correcting the understaffing problem, the problem still exists. In 1998, a 50% physician vacancy rate existed at one Navajo facility for 5 months. One hypothesis for the continued problem is that understaffing is a function of both recruitment and retention rates; if retention is excellent, recruitment rates will not necessarily affect staffing. However, if recruitment is excellent and retention is poor, a facility can remain understaffed. Therefore, efforts focused mainly on recruitment will not necessarily succeed.

Another explanation is that factors unique to a particular location may not be easily amenable to federal level intervention because individual facilities are increasingly responsible for their own recruitment and retention. Rates of understaffing vary between locations; some areas have ongoing 65% vacancy rates, and others have none.[2] An example of such a unique factor is that certain tribal authorities are taking control of the IHS unit in their area, with continued federal funding. This might influence staffing in particular areas, without any influence on other locations. Another example is that different IHS locations have different pay scales and financial incentives, although all physicians and midlevel providers are employees of the Public Health Service. Therefore, financial programs aimed at IHS physicians and midlevel providers as a whole may not address the needs of a particular service unit.

To determine what factors were associated with provider recruitment and retention in the Navajo Area, I conducted a survey of Navajo Area IHS physicians and midlevel health care providers. The Navajo Nation is unique in that it has more than 200,000 members and is the second largest in the country. Also, it is the largest geographically, covering more than 64,000 km^2 (>25,000 mi^2), the size of West Virginia.[3] The objectives of the survey were to determine what provider demographics and institutional variables were associated with both recruitment and retention. Questions examined factors in recruitment found to be significant in other surveys of physicians of underserved groups.[4-8] Also, the survey asked specifically about the effects of Public Law 93-638.[9] This federal law allows tribal authorities to manage their health care system with continued federal funding, and the

Navajo Nation plans to assume control of their system in the next 2 years.

METHODS

In mid-August 1998, the questionnaire was distributed to the clinical directors of all Navajo Area IHS facilities, who distributed it to physicians and midlevel health care providers in their facility. A preaddressed envelope was provided so that each provider could mail the survey directly without the clinical director seeing the response. Twelve facilities are listed as Navajo Area IHS facilities and range from outpatient clinic-only services to tertiary care centers; all serve rural communities. The questionnaire was developed in a focus group consisting of a physician at a Navajo Area IHS facility and the clinical directors; it was pilot-tested among the staff at a Navajo Area IHS facility. Eligibility was limited to health care professionals including physicians, nurse practitioners, physician assistants, nurse anesthetists, and midwives who were not under locum tenens contracts. Clinical directors were sent periodic reminders for their staff to finish the questionnaires. The surveys were collected until January 1, 1999.

The questionnaires were 3.5 pages long and began with questions on age, sex, race, marital status, number of children, upbringing in a rural or underserved area, the size of the community where they trained, degree, board certification, specialty, length of employ in the IHS and in the facility, number of hours worked, and amount of money still owed on medical school loans at the end of training. Participants were asked to rank on a 5-point Likert scale 36 factors that influenced their joining the IHS. They also were asked to rank by order of importance in fill-in-the-blank format the reasons they decided to join the IHS, if they planned to leave, and when. Finally, in order of importance, they were asked to list in a fill-in-the-blank format the reasons they decided to leave or stay.

The demographic characteristics of the participants were described using percentages for dichotomous variables. The characteristics of participants who planned to leave were compared with those who did not, using χ^2 tests for dichotomous variables. Also, characteristics of participants who planned to leave in the next 3 years were compared with those who planned to leave after that time and with those who planned to stay. To adjust for possible confounding, a multivariate logistic model was used to evaluate variables associated with plans to leave and when leaving was planned. Open-ended responses were coded, and the most common reasons listed for joining, staying, or leaving were tabulated. In 3 instances, the reasons for both leaving and staying were listed without a preference for leaving or staying, and these results were not used. All statistical tests were carried out using commercially available statistical software (STATA; Stata Corp, College Station, TX).

RESULTS

The clinical directors were asked how many staff members eligible to answer the questionnaire existed at each site, and these totaled 344; 221 staff members (64%) responded. We did not collect data on nonresponders because several of the IHS facilities had few physicians and midlevel providers, and there was concern about confidentiality of the responses. In all, 129 planned to leave, 89 planned to stay with their IHS facility, and 3 did not comment. Of those who planned to leave, 108 (48%) planned to do so in the next 3 years. Characteristics of the respondents and respondents who intend to leave within 3 years did not differ significantly by sex, race, marital status, presence of children, employment status of spouse, rural or underserved upbringing, completion of a residency, location of residency, specialty, loan burden, or a work week of more than 40 hours. Increased age ($P = 0.004$) and increased time spent in the IHS ($P = 0.01$) were significantly associated with plans to leave within the next 3 years. However, in a multivariate analysis, only age remained significant: if the provider was between 45 and 55 years old, they were less likely to leave than a person between 25 and 35 years old (odds ratio: 0.30; 95% confidence interval, 0.16-0.88). Response rates between different clinics did not vary significantly ($P = 0.06$).

Reasons for joining

When open-ended responses were tabulated, the most common reasons for joining the IHS were the desire to work in the southwestern United States, followed by the desire to work with the underserved, schedule flexibility, loan repayment, and variety in work content. These differed slightly from the reasons listed as those most influencing the decision to join as elicited from the Likert scales, which were desire to work with the poor, quality of the medical staff, job challenges, job variety, and recreational opportunities. Important reasons for joining on both the open-ended questions and Likert scales were the desire to work with the poor and the variety of work content. From the Likert scales, the most negative influences on joining were the quality of the schools, distance from family and friends, quality of administration, low salary, and lack of housing. From the median score and the percentage of responses above zero, a lack of jobs outside the IHS was not an important motivator to join.

Reasons to stay or leave

From the open-ended responses, the most common reasons to stay were the quality of the medical staff, schedule flexibility, desire to work in a rural area, desire to work in the Southwest, and the variety of work.

The most common reasons to leave were lack of administrative support and quality, fear of PL 93-638, dis-

tance from family and friends, excessive working hours, and the poor local school system. This did not vary significantly between different facilities in the IHS. The second most common reason for leaving was fear of PL 93-638 or the impending turnover of the Navajo Area IHS to the Navajo Nation. This fear was not elaborated on, and most often the comments stated that they did not know what to expect, although some were concerned that non-Navajo Native Americans would take their jobs or that a large drop in salary or negative change in benefits would occur.

Comments from physicians and midlevel providers

Although unsolicited, many physicians and midlevel providers elaborated extensively on their reasons to stay or leave. Because these comments come from unsolicited written responses on a survey with a fill-in-the-blank format, I did not subject them to formal qualitative coding.

The lack of housing was commented on by 10 respondents. One respondent summarized: "when one considers what physicians are being offered elsewhere, I think that fewer and fewer will be willing to accept the marginal housing facilities. Most of us come from an urban or community background and expect more. I know of young urban physicians who became very happy in rural settings [when adequate housing was provided]."

Lack of health care was also a negative influence, and one provider commented: "Health care is not provided for [those who are not] commissioned officers. It is insulting to new staff that we cannot provide basic health care for employees who are non-Native American. [These people] have to take an entire day of sick leave to go to a medical appointment, the nearest being 60 miles [away]."

Several physicians and midlevel providers who had worked in the IHS for more than a decade remarked that their situation had improved since they had started. One physician stated, "My generation of physicians has a hard time identifying with the concerns of younger physicians. Compared to years ago, work hours are much shorter, pay is much higher, educational and shopping opportunities are much greater, housing is more available and of better quality, etc."

Younger physicians agreed about the pay not being a problem in the decision to stay, although it did not encourage them to join. One stated, "Title 38 [institution of premium special pay for physicians] has made a huge difference; I make more money now than most of the other residents who finished at the same time as me." Physicians and midlevel providers who did not benefit from Title 38 stated that pay was inadequate. One nurse practitioner stated, "[We receive] no extra pay for hardship location when we live right next to medical doctors who get a bonus for same."

Although exceptions were noted, one provider wrote, "Administrators are 1. slow to adapt to change, 2. totally lack respect for physicians, and 3. should be replaced by trained persons rather than the usual 'on the job training' persons we've had." Another elaborated, "They are polite, but they manage to do absolutely nothing to make their nursing or medical staff feel appreciated. There is minimal communication regarding issues that directly impact on patient care; in fact, our opinions are never requested; and if we express them, we are perceived as threatening and hostile." This sentiment was also expressed by a provider who stated, "I am just a body, not a person to some." Poor administration was thought to contribute to increased administrative duties for physicians and midlevel health care providers and excessive hours. One respondent stated, "A big frustration was not being given administrative time on a regular, predictable basis."

DISCUSSION

This survey found that 108 (47%) of all Navajo IHS physicians and midlevel providers who responded to the survey planned to leave in the next 3 years. This low retention rate is lower than rates of retention in other rural health care facilities. In a 1992 survey, Pathman and colleagues found that roughly 25% of rural physicians not in the National Health Service Corps left their index practice and that about 80% left their index community after 3 years. Rates of retention for rural National Health Corps physicians were lower: about 20% remained in their index practice after 3 years, and about 40% remained in their index community.[4]

Concerning recruitment in 1998, Navajo Area IHS physicians and midlevel providers had personal reasons for joining, as indicated by their principal reasons for joining—desire to work with the poor and in the Southwest. However, institutional factors such as loan repayment, schedule flexibility, and work variety were important in recruitment. The attractions of the Navajo Area IHS and those cited as reasons for staying were similar and included the desire to work in the Southwest, the schedule flexibility, the variety of work, and the quality of the medical staff. These overcame concerns about the distance from family and friends, poor school quality, lack of easily accessible health care, comparatively lower salaries, and lack of housing.

The most common reasons cited for leaving, however, were institutional, such as lack of administrative support, quality and fear of impending tribal management, and excessive working hours. Other factors were environmental and located outside the IHS, such as the local school system. These findings are similar to those of a 1992 report examining understaffing in the IHS that found high vacancy rates due to inferior pay, "community and environment factors," and "administrative support."[2]

This survey has several limitations. Because no easily accessible statistics exist on health care professionals on the

Navajo reservation, there is little information on nonresponders. Thus, respondents may not be representative of health care professionals on the reservation as a whole, despite the high 64% response rate. Also, we do not know how the respondents' answers corresponded with their decisions to stay on the reservation. Finally, themes could have been further clarified with more qualitative analysis. Particularly, further discussion of dissatisfaction with the administration may have yielded more specific and potentially amenable reasons.

Many unique factors draw applicants to the Navajo Area IHS, including the southwestern US location and work content variety. The rapport with the medical staff often encourages physicians and midlevel providers to stay. These reasons are not enough, however, to stem an efflux of physicians and midlevel providers, an estimated 47% in 3 years. Unique issues to the Navajo Area IHS are important in physicians and midlevel providers' intention to leave, such as the fear of Title 638, whereas factors such as low pay are not as important as in other areas. Further qualitative research on provider focus groups that emphasized confidentiality of responses would help clarify themes of dissatisfaction and possibly identify solutions.

I thank the participants of the survey for their time and effort and Dr Douglas Peter.

At the time this survey was done, Dr Kim was affiliated with the Crownpoint Healthcare Facility, Crownpoint, NM.

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COMMENTARY

How long will you be staying, Doctor?

The data presented in Kim's study can be applied at 3 levels: within the Navajo area, within the Indian Health Service (IHS) as a whole, and within all of rural America. There are important lessons to be learned at each level.

The Navajos live in a large and beautiful, if barren, reservation encompassing parts of Arizona, New Mexico, and Utah. Partly for this reason, and partly because their ancestral culture is maintained more than in some other cultures of Indian country, recruiting to the Navajo area has been less difficult than to other parts of the IHS. Kim notes, however, that "if recruitment is excellent and retention is poor, a facility [or an area] can remain understaffed."

When I arrived in Gallup, New Mexico, at the edge of the Navajo Reservation, as a new general medical officer in 1970, I was asked not "Where were you trained?" or "What is your philosophy of care?" but "How long will you be staying, Doctor?" Despite having been served by a succession of well-trained, enthusiastic, and altruistic physicians, my patients were concerned about seeing another new entrant coming through the revolving door.

Kim's data have important messages for the IHS and for the Navajo tribe before and after the tribe assumes control of its health care system. The IHS spends considerable money and effort in recruiting to Navajo facilities; it should spend considerable effort in retaining its many good providers. Where administrators are perceived as being unresponsive and unappreciative of the physicians in their facility and the needs of their families, the reality and the perception can be changed. The IHS could also make a strong effort to convince its providers that changeover to tribal control of the health system will be a positive experience, as has been the case in many other parts of the IHS—for example, in most of Alaska, in Chickasaw and Choctaw portions of Oklahoma, and in Warm Springs, Oregon (R Gollub and J Berner, oral communications, July 2000). The tribe could specifically address the issue of making health care available to its non-Indian employees, as it is empowered to do under PL 93-638. It is more difficult to see an easy solution to the "quality of schools" issue.

Assuming that the Navajo tribe wishes to retain most of the physicians by whom it is served, it, too, could be more reassuring regarding its intentions to retain and to adequately compensate those physicians. It could signal its intentions even before its takeover of the health system by dealing with the severe housing problem at many of its facilities.

Bolte studied questionnaire results from 283 of the

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approximately 800 IHS physicians across the country.[1] Her findings are similar to Kim's in many respects (although dealing only with physicians). With respect to national IHS retention problems, Kim's and Bolte's findings are salient. Some factors are beyond easy IHS control, such as the availability of good schools and recreational and cultural activities. Some, however, could be given greater attention, such as housing, responsiveness of administrators to providers' concerns and family needs, adequate compensation, and professional education. Everling cites 10 scholarship or loan programs available to the IHS for the purpose of recruiting and retaining medical providers[2]; the only one having to do with providing continuing medical education funds has not been funded by Congress since 1978.

Roemer catalogues other countries' methods of dealing with rural health needs.[3] In the United States, problems with maldistribution of physicians (away from high-need areas such as rural regions) have been thoroughly discussed over the past decades. Programs such as the highly successful Physician Shortage Area Program (PSAP) at Jefferson Medical College in Philadelphia have done well by specifically recruiting students from rural areas who express the desire to return there and by providing a substantial portion of their education in rural areas.[4] The retention of PSAP graduates has also been good. The IHS similarly invests a large amount of effort and money in recruiting Native American students into medical fields, assuming that they, too, will return to serve their tribes.[4] Burnett and colleagues note that family practice residency programs have in general been most successful at routing graduates to rural areas.[5] Among the reasons they give is that "family practice residency programs often are structured specifically to prepare physicians in ambulatory settings in communities for which there are access barriers (geographic, social, or economic)."

Other residency programs could make similar efforts to convince students and house staff of the benefits of a rural practice. This would aid recruitment. Employers recruiting physicians to rural communities will find lessons in Kim's data in how to retain them. While "I'm planning to stay forever!" might not be the answer always given to a rural resident, Native American or otherwise, such attention to the details of the life of rural medical providers would improve the chances that they would stay "a long time!"

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Medical malpractice: the effect of doctor-patient relations on medical patient perceptions and malpractice intentions

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ABSTRACT **Objective** To examine the causal effects of doctor-patient relations and the severity of a medical outcome on medical patient perceptions and malpractice intentions in the event of an adverse medical outcome. **Design** Randomized between-subjects experimental design. Patients were given scenarios depicting interactions between an obstetric patient and her physician throughout the patient's pregnancy, labor, and delivery. **Participants** One hundred twenty-eight postpartum obstetric patients were approached for participation, of whom 104 completed the study. **Main outcome measures** Patients' perceptions of physician competence and intentions to file a malpractice claim. **Results** Positive physician communication behaviors increased patients' perceptions of physician competence and decreased malpractice claim intentions toward both the physician and the hospital. A more severe outcome increased only patients' intentions to sue the hospital. **Conclusion** These results provide empiric evidence for a direct, causal effect of the doctor-patient relationship on medical patients' treatment perceptions and malpractice claim intentions in the event of an adverse medical outcome.

In the past 30 years, medical malpractice has become 1 of the most difficult health care issues in the United States. In addition to billions of dollars in legal fees and court costs, medical malpractice premiums in the United States total more than $5 billion annually,[1] and "defensive medicine"—procedures performed to protect against increasing

litigation—is estimated to cost more than $14 billion a year.[2] In addition, although most claims do not result in awards, being involved in a malpractice suit is often a personally and professionally devastating experience.[3-6] Studies have repeatedly shown that the quality of medical care alone is a poor predictor of a medical malpractice claim,[7-14] and researchers have argued that the rapport between physicians and their patients is a principal determinant of patients' evaluation of their treatment.[5,15-19]

In examining this doctor-patient hypothesis, recent research has found that physicians who exhibit more negative communication behaviors are more likely to have been sued in the past for malpractice than those with more positive doctor-patient relations.[20,21] Although these data demonstrate associations between doctor-patient relations and malpractice claims, they do not indicate that rapport caused these differences in claims against physicians. Rather, past experience with malpractice claims may have affected physicians' subsequent interactions with their patients. Thus, there remains a need, as noted by Slawson and Guggenheim, "to find a way to demonstrate the likelihood that most suits brought against physicians are caused by a breakdown of doctor-patient relationships."[22(p981)]

The most effective method for identifying causal relationships is an experimental design in which participants are randomly assigned to systematically controlled conditions. In the only experimental examination of the doctor-patient hypothesis, researchers showed students a videotape of a hypothetic office visit between a dermatologist and his patient that resulted in either discomfort or scarring.[23] The study found that negative physician communication decreased perceptions of physician competence and raised expressed intention to file a malpractice claim. However, the length of the office visit differed significantly between the positive and negative communication conditions. In addition, whether this research with students would generalize to actual medical patients is unclear.

Malpractice claims may be more likely in cases where clinical outcomes are more severe. Although more severe outcomes are associated with higher monetary awards to malpractice plaintiffs,[24] the direct effects of outcome severity on patients' intention to file a malpractice claim have not been examined. We, therefore, wished to address 2 research questions in our study. First, are malpractice claims more likely when the clinical outcome is more severe? Second, are these affected by the quality of the doctor-patient relationship?

SUBJECTS AND METHODS

Participants

Participants were 104 obstetric patients at a major university medical center, for whom institutional review board approval was obtained before the research began. Patients ranged in age from 18 to 45 years, with a mean age of 32 years. All patients had borne a child in the previous 6 to 12 months. Fifty-nine participants (57%) were white, 18 (17%) were Latina, 11 (11%) were Asian, 9 (9%) were African American, and the rest (6%) were from other ethnic backgrounds. Three participants (3%) had not completed high school, 27 (26%) were high school graduates, 42 (40%) were college graduates, and 32 (31%) had earned graduate degrees.

The core scenario describes the pregnancy, labor, and delivery of a woman, Jane Larsen, giving birth to her first child, including her interactions with her obstetrician, Dr David Miller. The scenario begins with Jane's initial office visit (for which Dr Miller is 30 minutes late), which includes a comprehensive health history and physical examination. Follow-up visits typically include a brief physical examination, measurement of the baby's heart rate, and a discussion of any changes Jane has noticed since her last visit. During the final 2 months of the pregnancy, Dr Miller reviews the labor and delivery process. Jane feels contractions beginning soon after the 38th week of pregnancy, at which point she phones Dr Miller and is admitted to the hospital. After Jane has undergone 5 hours of labor in the hospital, her contractions suddenly become abnormally strong and frequent. An anesthetic is administered to reduce the intensity of the contractions, but to little effect. The fetal heart rate then begins to decrease rapidly, at which point Dr Miller performs a cesarean section.

Procedure

Participants were chosen from patients at the University of California, San Francisco, Obstetrics and Gynecology Faculty Practice. We chose to study obstetric patients because they are among the most likely to file malpractice claims in the event of an adverse medical outcome.[19] Prospective participants were identified by medical records review, and only women who had delivered healthy babies in the previous 6 to 12 months were contacted. Patients who did not speak English and those with a history of either psychological problems or drug addiction were not considered for participation.

A preliminary power analysis was conducted to determine the necessary sample size for this 2-factor analysis of variance. A power of 0.80 was assumed, and an α of 0.05 was chosen. To detect a moderate effect (Pearson product moment $r = 0.30$), a minimum sample size of 82 participants was required.[25] Given an expected refusal rate of 25% and a questionnaire return rate of 85%, a total of 128 postpartum women were contacted for participation.

Women who met the inclusion criteria were contacted by phone and asked if they would participate in a study involving the opinions of recent mothers about various aspects of pregnancy. Of 128 women who were contacted, 123 agreed to participate in the study, each of whom was then mailed a study packet. Each packet included a cover

letter (providing a brief introduction and directions), a consent form, and the study instrument containing a scenario and response questionnaires. A total of 104 women subsequently completed and returned the materials. No significant differences were found between respondents and nonrespondents in age, ethnicity, education, length of pregnancy, or postpartum hospitalization. In addition, the rate of return for questionnaires did not differ significantly across experimental conditions.

Study scenarios

The study instrument presented to each patient included 1 of 4 scenarios depicting the interactions between an obstetric patient and her physician throughout the patient's pregnancy, labor, and delivery. Based on interviews with physician members of the Obstetrics and Gynecology Faculty Practice, each scenario included a common core scenario, in addition to elements specific to its experimental condition. Each participant was asked to respond as if she were in the position of the patient described. An example of a case scenario is shown in the box.

Experimental conditions

Two factors were included in the current research design. Two levels of doctor-patient relations (positive or negative) were combined with 2 levels of medical outcome severity (mild or severe) to comprise a 2 × 2 between-subjects experimental design. A randomly ordered series of integers from 1 to 4 was used to assign each participant to 1 of the 4 experimental conditions.

Doctor-patient relations

The quality of doctor-patient relations was varied according to physician communication behaviors. Among pilot study patients, 7 physician communication behaviors emerged as most important for doctor-patient rapport. These behaviors included whether the physician was friendly, personally interested in the patient, emotionally supportive, communicated clearly, let the patient know what to expect, confirmed patient understanding, and offered suggestions to make the pregnancy easier. Using pilot information gained from both physicians and patients, specific examples of these behaviors (summarized in table 1) were inserted throughout each scenario.

Medical outcome severity

Immediately following the description of the labor and delivery, a final paragraph indicated the severity of the medical outcome for the newborn child. In all scenarios, this paragraph began with the following sentence: "Soon after the birth, it was determined that the baby had experienced ischemia (sharply reduced blood flow) and asphyxia (a lack of oxygen) as a result of these complications."

Table 1 *Positive and negative physician communication behaviors*

Behavioral categories	Specific communication behaviors: Positive	Specific communication behaviors: Negative
Friendly	Greeted patient warmly Apologized for delay	Did not greet patient Did not apologize for delay
Personal interest in patient	Asked informal questions Gave patient undivided attention Made eye contact	Asked no informal questions Always seemed in a hurry to finish Made no eye contact
Emotionally supportive	Praised patient for quitting smoking during pregnancy Offered condolences on death of patient's father Never critical when making recommendations	Admonished patient for having smoked before pregnancy No repsonse to death of patient's father Often critical when making recommendations
Provided explanations	Explained changes patient experienced during pregnancy Pointed out possible obstacles to patient adherence	Did not explain changes patient experienced during pregnancy Did not point out any obstacles to patient adherence
Communicated clearly	Rarely used medical terms Explained terms when used	Often used medical terms Did not explain terms
Confirmed understanding	Encouraged patient to ask questions Listened carefully to patient	Did not encourage questions Interrupted patient frequently
Made suggestions to make pregnancy easier	Offered referral for counseling Provided strategies for overcoming obstacles to adherence	Did not offer counseling referral Provided no strategies for overcoming obstacles to adherence

The final sentence then determined the outcome severity conditions. In the mild outcome conditions, the baby was said to have "a slight chance of experiencing some developmental problems or long-term mental impairment, [but] this was very unlikely because most babies who suffer mild asphyxia live perfectly normal lives." In the severe outcome conditions, patients read that further tests "indicated that the infant had almost certainly suffered serious brain damage, which would lead to significant developmental problems, as well as long-term mental retardation."

Patient response measures

Patient satisfaction

To measure patient satisfaction with the depicted physician, participants completed the Patient-Doctor Interaction Scale (PDIS), a standardized questionnaire designed to assess patients' perceived quality of treatment by a physician.[26] The PDIS has undergone extensive validation and is frequently used to measure medical patient satisfaction.[27] It consists of 18 items, half of which are framed positively (eg, "The doctor explained the reasons for his recommendations") and half negatively (eg, "The doctor used many words I did not understand"). Participants indicated the extent to which they agreed with each statement on a scale from 1 ("strongly disagree") to 5 ("strongly agree"). After negatively framed items were reverse-scored, responses were combined and averaged, resulting in an overall score for each participant that ranged from 1 to 5, with higher numbers representing greater satisfaction. In the current context, this measure provides a check on the effectiveness of the doctor-patient conditions. For this reason, patients were presented with the PDIS immediately before the description of labor and delivery. In addition, participants were asked to complete each section of the study before beginning the next section.

Patient perceptions

Using the same 1-to-5 scale (strongly disagree to strongly agree), patients indicated their beliefs about the competency of the physician described in the scenario, the predictability of the complications associated with the births, and the physician's responsibility for the outcome. Specifically, participants indicated their agreement, respectively, with the following statements: "The doctor was competent," "The complications of the birth were predictable," and "The doctor was responsible for the complications of the birth." To obtain more detailed information about patients' perceptions of responsibility, the questionnaire also asked participants to indicate the percentage of responsibility (from 0%-100%) they attributed to the physician, the patient herself, the nursing staff, and chance.

Malpractice claim intentions

Finally, again using a 5-point scale, patients indicated their agreement with the statement, "Given what happened in the pregnancy described earlier, I would be likely to file a malpractice claim against the physician." Using the same scale and type of question, patients then indicated the likelihood that they would file a malpractice claim against the hospital.

RESULTS

Preliminary analysis

To examine the effectiveness of the current randomization, we conducted preliminary analyses comparing participant demographic variables across experimental conditions. No significant differences were found between any of these conditions in either participant age, ethnicity (white vs nonwhite), or years of education ($P>0.46$ for all variables).

Table 2 *Mean patient satisfaction, physician competence, outcome predictability, physician responsibility, and malpractice intentions for positive and negative physician communication*

Response measure	Overall rating	Total No.	Positive communication	No.	Negative communication	No.
Satisfaction†	2.80 (1.17)	104	3.81 (0.67)	52	1.80 (0.52)	52
Physician competence‡	2.70 (1.28)	101	3.06 (1.32)	50	2.35 (1.16)	51
Outcome predictability	3.24 (1.25)	102	3.08 (1.31)	51	3.39 (1.18)	51
Physician responsibility§	3.21 (1.30)	103	2.82 (1.20)	51	3.60 (1.30)	52
Malpractice intentions						
Against physician†	3.12 (1.34)	103	2.55 (1.15)	51	3.67 (1.28)	52
Against hospital§	3.45 (1.29)	102	3.16 (1.27)	52	3.73 (1.25)	50

†Significant difference between positive and negative behaviors ($P = 0.001$).
‡Significant difference between positive and negative behaviors ($P = 0.01$).
§Significant difference between positive and negative behaviors ($P = 0.05$).

Patient satisfaction

Participants expressed an overall mean satisfaction rating of 2.8 out of a possible 5.0 (table 2). Patients presented with positive physician communication behaviors expressed significantly greater satisfaction (mean = 3.8) than those exposed to more negative physician behaviors (mean = 1.8; $F_{1,103} = 291.39$, $P<0.001$). Patients' expressed satisfaction did not differ significantly with the severity of the medical outcome ($P>0.34$) or the interaction between outcome severity and communication behaviors ($P>0.90$).

Physician competence

Patients gave the physician an overall mean competency rating of 2.7. Participants presented with positive communication behaviors reported significantly greater perceptions of physician competence (mean = 3.1) than those exposed to more negative behaviors (mean = 2.3; $F_{1,100} = 8.13$, $P<0.01$). Neither the severity of the medical outcome ($P>0.45$) nor its interaction with physician communication behaviors ($P>0.70$) exerted a significant influence on participants' perceptions of physician competence.

Event predictability

On a scale from 1 to 5, participants rated the predictability of the medical complications as 3.2. This rating did not differ significantly as a function of either doctor-patient relations, outcome severity or their interaction ($P>0.31$ for all).

Physician responsibility

On average, patients attributed 44% of the responsibility for the adverse medical outcome to the physician, 7% to the hospital staff, 10% to the patient herself, and 39% to chance. Patients exposed to positive doctor-patient relations ascribed less responsibility to the physician for the adverse outcome (mean = 2.8) than those presented with less positive relations (mean = 3.6; $F_{1,102} = 9.65$, $P<0.01$). The severity of the medical outcome exerted no influence on any patient perceptions of responsibility ($P>0.54$), and the effect of outcome severity was not influenced by the quality of the doctor-patient communication ($P>0.65$).

Malpractice claim intentions

Patients' overall average claim intentions toward the physician and the hospital were, respectively, 3.1 and 3.5 on a 5-point scale. With positive doctor-patient relations, patients reported significantly lower malpractice claim intentions toward both the physician ($F_{1,102} = 21.97$, $P<0.001$) and the hospital ($F_{1,101} = 5.61$, $P<0.05$). However, a more severe outcome increased only patients' intentions to sue the hospital ($F_{1,101} = 8.59$, $P<0.01$) (table 3). Finally, the effect of doctor-patient relations on patient malpractice claim intentions was independent of the severity of the adverse medical outcome ($P>0.36$).

DISCUSSION

Positive doctor-patient relations increased obstetric patients' perceptions of physician competence, decreased their perceptions of physician responsibility for an adverse medical outcome, and reduced their expressed intentions to file malpractice claims against both the physician and the hospital. Outcome severity affected only expressed malpractice intentions toward the hospital, and the interaction between doctor-patient relations and outcome severity exerted no detectable effect on any outcome measures in the current study.

This research has several limitations. First, obstetric patient responses may not generalize to medical patients as a whole, as illustrated by research findings that malpractice claims against surgeons were not associated with the quality of their communication behaviors.[21] Although this effect may reflect the gender of these surgeons (all but 1

Table 3 *Mean patient satisfaction, physician competence, outcome predictability, physician responsibility, and malpractice intentions for mild and severe medical outcomes*

Response measure	Overall rating	Total No.	Mild medical outcome	No.	Severe medical outcome	No.
Satisfaction	2.80 (1.17)	104	2.89 (1.14)	52	2.72 (1.21)	52
Physician competence	2.70 (1.28)	101	2.80 (1.26)	49	2.62 (1.32)	52
Outcome predictability	3.24 (1.25)	102	3.06 (1.20)	50	3.40 (1.29)	52
Physician responsibility	3.21 (1.30)	103	3.13 (1.33)	52	3.29 (1.29)	51
Malpractice intentions						
Against physician	3.12 (1.34)	103	2.96 (1.37)	51	3.27 (1.30)	52
Against hospital*	3.45 (1.29)	102	3.10 (1.37)	51	3.80 (1.10)	51

*Significant difference between mild and severe medical outcomes ($P = 0.01$).

of whom were men), the doctor-patient hypothesis may also be particularly relevant to medical services that, like obstetrics, involve ongoing doctor-patient relationships. These questions can be addressed by future research comparing responses from patients with male with those with female physicians within different medical specialties.

Second, participants in this study were not involved in the cases to which they responded, which may help to explain the modest effects of outcome severity. However, a more severe outcome did increase participants' litigious intentions toward the hospital, indicating some effect of these severity conditions. Moreover, doctor-patient relations exerted significant effects, which presumably would have been even more pronounced had patients actually been involved in the case.

Third, the current research involved patients' expressed malpractice intentions rather than actual behavior. Although intentions do not necessarily translate into behavior, in the context of malpractice decision making, they are a necessary precursor to action. Thus, to the extent that positive doctor-patient relations reduce malpractice intentions, they may similarly influence the eventual decision to file a claim.

Finally, the current participants were of relatively high socioeconomic status. Medical patients with higher levels of education have reported less satisfaction than patients with lower levels of education,[28] and wealthier patients are more likely to file malpractice claims than those with lower incomes.[29] Thus, although these participants may not be representative of patient populations at large, higher socioeconomic status may be particularly relevant to medical malpractice claims.

The current results support the notion that physicians' interpersonal interactions with patients—apart from the technical care they provide—is a critical aspect of patient care. In addition, although a more serious medical outcome may not make patients more inclined to file a claim against a physician, a less severe outcome may not be sufficient to prevent a claim when the doctor-patient relationship is poor.

The method used in the present research—experimental conditions embedded in scenarios presented to actual patients—is provided as a model for future studies seeking to test the doctor-patient hypothesis, and to identify other determinants of patient satisfaction, perceptions, and other outcomes. For example, the effects of doctor-patient relations found in this and other studies may be attributable to a relatively small subset of behaviors of particular importance to patients. This possibility can be evaluated in future experiments by systematically examining specific communication behaviors, both individually and in combination. The results of such research can help us better understand and address the needs of medical patients, including those whose outcomes may be poor. In turn, this information can be used to reduce patient stress, potential litigation, and the tremendous costs associated with each, both for those involved and for society as a whole.

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COMMENTARY

Communication: it is common sense

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Moore and colleagues present a challenge to all who are responsible for patient care, and they contribute objective evidence to support the importance of what seems inherently obvious: in a single word, "respect." Patients treated with respect are more satisfied with their physicians and other care providers, irrespective of the outcome. Furthermore, satisfied patients are less likely to seek legal recourse following an adverse event.

This message should not surprise anyone. It is simply common sense, especially when considering patients as customers or clients. The idea of the importance of respect reaches beyond the confines of medicine and permeates all of society. Whether with an automobile mechanic, a real estate agent, or a sales associate at a retail store, the quality of an encounter consciously and subconsciously influences our satisfaction with the experience. Dissatisfaction may lead to frustration and anger that ultimately manifests as a complaint or claim.

By legal standards, medical malpractice requires the presence of a physician-patient relationship that establishes the duty of care, an adverse outcome (injury or harm), negligence by the provider (failure to meet the standard of care based on local standards), and direct causality between the negligence and the adverse outcome. However, the legal basis for malpractice remains silent on a critically important component: the dissatisfied, angry "customer."[1] We may reasonably conclude that with increased satisfaction, fewer claims would be filed, and financial resources could be better directed toward patient care rather than legal fees.

Risk managers and educators should view this evidence as an opportunity. Traditionally, health care management has employed a reactionary stance to claims management, with less emphasis on strategies to reduce risk. The focus on claims management potentially limits opportunities to minimize malpractice exposure. Risk managers should be rewarded for placing increased emphasis on helping their organizations' providers improve doctor-patient communication skills during all patient encounters, not just following an adverse event. In an effort to be increasingly proactive, many academic centers and medical schools have embraced the idea of training the next generation of physicians to provide care that is compassionate, humanistic, high quality, and evidence-based.[2] This is done with the logical hope that the patients of physicians who embrace and value the importance of the doctor-patient relationship will be more satisfied with their care, irrespective of the outcome. As a result, patients are more likely to follow their physicians' recommendations,[3] have better clinical outcomes, and be less likely to seek legal avenues to express anger and dissatisfaction.

A recent Institute of Medicine report, *To Err Is Human: Building a Safer Health System,* reminds physicians that they are all prone to error.[4] Medicine, as everyone knows, is not an exact science. Unfortunately, errors in procedure, technique, judgment, and communication may all result in temporary or permanent harm to patients. Although the threat of an impending lawsuit following an adverse outcome will always exist, health care providers would be wise to buffer themselves from these threats. The article by Moore and associates suggests that a good physician-patient relationship is effective in reducing malpractice claims. Perhaps more physicians would benefit if they spent more energy developing effective and positive interaction skills.

Maybe physicians need reminding of the golden rule, "Do unto others as you would have them do unto you." This rule applies as much to physicians' relationships with patients as to anything else in everyday life. Respect is not just about addressing a patient by a title such as "Ms" or "Sir"; it also involves understanding patients' hopes, dreams, wants, needs, and emotions and making an effort to specifically address those issues. And as patients, we would expect nothing less.

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Journal Digest

Is a clinical prediction model accurate for predicting ectopic pregnancy?

Buckley RG, King KJ, Disney JD, et al. History and physical examination to estimate the risk of ectopic pregnancy: validation of a clinical prediction model. *Ann Emerg Med* 1999;34:589-594

QUESTION

In women with abdominal pain or vaginal bleeding in the first trimester of pregnancy, how accurate is a clinical prediction model for predicting ectopic pregnancy?

DESIGN

Two cohort studies: 1 for derivation and 1 for validation of the clinical prediction model results.

SETTING

The emergency department of a military tertiary-care teaching hospital in San Diego, California.

PATIENTS

Women who were hemodynamically stable and had abdominal pain or vaginal bleeding in the first trimester of pregnancy. Exclusion criteria were previous documentation of an intrauterine pregnancy (IUP) on pelvic ultrasonography, enrollment in the prospective clinical data registry on a previous visit to the emergency department, or estimated gestational age and corresponding uterine size of 13 weeks or more. A total of 486 women (mean age 25 years and mean gestational age 58 days) formed the derivation cohort, and 429 women (mean age 25 years and mean gestational age 58 days) formed the validation cohort.

DESCRIPTION OF PREDICTION GUIDE

The clinical prediction model classified pregnant women into 3 groups according to risk. High-risk women had signs of peritoneal irritation or definite cervical motion tenderness; intermediate-risk women had no fetal heart tones by handheld Doppler ultrasonography, no tissue visible at the cervical os, and no pain (other than midline suprapubic cramping) or tenderness (any cervical motion or uterine or adnexal tenderness); and low-risk women did not meet high- or intermediate-risk criteria.

MAIN OUTCOME MEASURE

Diagnosis of IUP or ectopic pregnancy.

MAIN RESULTS

In the derivation cohort, 282 women (58%) had a viable IUP, 165 (34%) had a nonviable IUP, and 39 (8%) had an ectopic pregnancy. In the validation cohort, 266 women (62%) had a viable IUP, 129 (30%) had a nonviable IUP, and 34 (8%) had an ectopic pregnancy. Sensitivities, specificities, and likelihood ratios are shown in the table.

CONCLUSION

In women with abdominal pain or vaginal bleeding in the first trimester of pregnancy, the high-risk criteria of a clinical prediction model had high specificity but low sensitivity, and the intermediate-risk criteria had high sensitivity but low specificity for predicting ectopic pregnancy.

Commentary

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Buckley and colleagues explored the use of a clinical prediction model in the diagnosis of ectopic pregnancy among women with complicated first-trimester pregnancies. Criteria from the model that were useful—that is, signs of abdominal or pelvic peritoneal irritation and the presence of either fetal heartbeats or products of conception at the cervical os—revealed only the obvious cases and were seen too infrequently to influence management in most patients.

The authors state that incorporating historical risk factors in the model, such as exposure to previous tubal surgery, did not improve its accuracy, although these data were not analyzed in the report. This finding is strange unless these women were underrepresented through selection and received prenatal care elsewhere. They obviously have a higher risk for ectopic pregnancy than unexposed women, a factor that increases the probability of ectopic pregnancy once they are symptomatic.[1,2]

This finding probably does not affect the generalizability of the model to other emergency departments. A previous study of patients in an obstetrics and gynecology setting confirmed the limitations of physical findings in diagnosing ectopic pregnancy.[3] The study by Buckley and associates underlines the need for diagnostic expertise and equipment—transvaginal ultrasonography and serum human chorionic gonadotropin testing—for any unit responsible for managing women with complicated first-trimester pregnancies.

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Test characteristics of a clinical prediction model for predicting ectopic pregnancy

Risk status	Sensitivity (95% CI)*	Specificity (CI)*	+LR	−LR
High risk	32 (17-49)	95 (92-97)	6.1	0.7
Intermediate risk	100 (84-100)	28 (23-32)	1.4	0

CI = confidence interval; LR = likelihood ratio.
*Data are given as percentage.

Is hyaluronic acid effective in patients with osteoarthritis of the knee?

Huskisson EC, Donnelly S. Hyaluronic acid in the treatment of osteoarthritis of the knee. *Rheumatology* 1999;38:602-607

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Competing interests:
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QUESTION

In patients with osteoarthritis of the knee, is hyaluronic acid effective in relieving symptoms?

DESIGN

Randomized (unclear allocation concealment), blinded, placebo-controlled trial with 6-month follow-up.

SETTING

A hospital outpatient clinic in London, England.

PATIENTS

One hundred patients (mean age 65 years, 67% of whom were women) who had osteoarthritis of 1 or both knees according to the criteria of the American Rheumatism Association, changes in osteoarthritis (Kellgren and Lawrence grade II or III) on radiography in the previous 6 months, consistent pain in the previous 3 months, and moderate or severe pain on walking. Exclusion criteria were grade IV changes on radiography, functional impairment of the knee, associated osteoarthritis of any other joint that might affect assessment of the knee, psoriasis, other joint diseases or infection, other painful knee conditions, serious medical illness, skin conditions overlying the joint, or intra-articular use of steroids or radiocolloids in the previous 3 months. Follow-up at 6 months was 81%.

INTERVENTION

Patients were allocated to receive hyaluronic acid, 20 mg in 2 mL of aqueous solution (n = 50), or placebo (n = 50), given in 5 weekly intra-articular injections.

MAIN OUTCOME MEASURES

Knee pain on walking (100-mm visual analog scale) and knee function (Lequesne functional index).

MAIN RESULTS

Patients in the group receiving hyaluronic acid had less pain on walking at 5 weeks ($P = 0.009$) and 6 months ($P = 0.005$) than did patients in the placebo group (table). Knee function was more improved in the hyaluronic acid group at week 5 than in the placebo group ($P = 0.04$); the difference persisted to 4 months (table).

*Hyaluronic acid (HA) versus placebo for osteoarthritis of the knee**

Outcomes	Mean scores HA	Mean scores Placebo	Mean score difference (95% CI)
Walking pain at 5 wk	27.5	40.6	13.1 (1.4-24.8)
Walking pain at 6 mo	39.4	53.7	14.9 (1.4-27.2)
Knee function at 5 wk	10.0	12.1	2.1 (0.2-4.0)
Knee function at 4 mo	10.2	12.4	2.2 (0.2-4.2)

CI = confidence interval.
*Mean scores obtained from 100-mm visual analog scale and Lequesne functional index. Mean score differences favor the HA group.

CONCLUSION

In patients with osteoarthritis of the knee, hyaluronic acid was effective in reducing pain on walking at 6 months and improving knee function for 4 months.

Commentary

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Management of symptomatic osteoarthritis includes the use of nonsteroidal anti-inflammatory drugs (NSAIDs) or intra-articular corticosteroids (or both), viscosupplementation, and ultimately total knee arthroplasty. In a well-executed, randomized, placebo-controlled trial, Huskisson and Donnelly have shown that viscosupplementation with a course of 5 weekly hyaluronic acid (Hyalgan) injections can relieve pain for 6 months and improve function for 4 months in relatively healthy patients with a mean age of 66 years. This study showed that the beneficial effect is at least as good as that achieved with NSAIDs but without the gastrointestinal effects.

Whereas hyaluronic acid requires 5 injections,[1] hylan G-F 20 (Synvisc), another viscosupplementation agent, is effective after 3 weekly injections.[2,3] Findings show that courses of hylan G-F 20 injections can be repeated every 6 months and may thus provide relief for several years.[3] The study by Huskisson and Donnelly showed that injection site pain and local reactions may occur in up to 30% of patients receiving hyaluronic acid, but such adverse effects are also common with placebo injections.[1] The lateral approach with a straight knee results in the fewest problems.[3]

The precise indications for viscosupplementation remain somewhat controversial, although patients with early arthritis and moderate symptoms seem to gain the most benefit from this intervention.

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Are spacers made from sealed cold-drink bottles as effective as conventional spacers?

Zar HJ, Brown G, Donson H, et al. Home-made spacers made from sealed-cold drink bottles were as effective as conventional spacers in children with acute asthma. *Lancet* 1999;354:979-982.

QUESTION

In children with acute asthma, are homemade spacers as effective as conventional ones for improving response to a β_2 agonist given by metered-dose inhaler?

DESIGN

Randomized (allocation concealed), blinded, controlled trial with 15- to 30-minute follow-up.

SETTING

A children's hospital in South Africa.

PATIENTS

Eighty-eight children, 5 to 13 years of age (mean age 10 years), 53 (60%) of whom were boys and 44 (50%) of whom had moderate to severe airway obstruction (peak expiratory flow rate 20%-59% of predicted normal value), with a history of asthma, who presented with acute asthma. Exclusion criteria were the inability to use a metered-dose inhaler and spacer or to have pulmonary function tests, having a peak expiratory flow rate of less than 20% of the predicted normal value, an arterial oxygen saturation of less than 92% (as measured in room air), or cardiac or other chronic pulmonary disease; the recent use of oral corticosteroids; or the use of β_2 agonists within 4 hours of presentation. Follow-up was 100%.

INTERVENTION

Children were allocated to 1 of 4 types of spacers: a conventional spacer (Aerochamber; Trudell Medical, Canada) (n = 22); a 500-mL plastic cold-drink bottle with glue to seal the joint between the metered-dose inhaler and bottle (n = 22); an unsealed, 500-mL plastic cold-drink bottle (n = 22); and a 200-mL polystyrene cup (n = 22). Children received fenoterol hydrobromide, 100 µg per puff, in a metered-dose inhaler and spacer, 1 puff every 10 seconds. Children who weighed 25 kg or less (≤55 lb) received 400 µg; those who weighed more than 25 kg received 600 µg.

MAIN OUTCOME MEASURES

Changes in clinical score and pulmonary function and need for nebulization.

MAIN RESULTS

Analysis was by intention to treat. An improvement in lung function was seen in all groups. Results for the sealed bottle group were similar to those for the conventional spacer group; a cup was least effective ($P = 0.02$). Among children with mild airway obstruction, clinical scores, pulmonary function, and need for nebulization did not differ among study groups.

Among children with moderate to severe airway obstruction, clinical scores did not differ among study groups, and a cup was least effective for improving pulmonary function ($P < 0.05$). In children with moderate to severe obstruction, nebulization was needed by 10 of 11 children who used a cup, 9 of 11 who used an unsealed bottle, 8 of 11 children who used a sealed bottle, and 4 of 11 who used a conventional spacer.

CONCLUSION

In children with acute asthma, spacers made from sealed cold-drink bottles were as effective as conventional spacers.

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Competing interests: None declared

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Commentary

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The study by Zar and colleagues was a well-designed, randomized, controlled trial—the gold standard for evaluating therapeutic methods. It shows that adequate medication delivery for asthma can be achieved with both expensive and inexpensive tools.

Overall, the results have practical implications for asthma guidelines in developing and industrialized countries. Some programs allow replacement of spacers only once every 2 years. Spacers may also be the only alternative for delivering non-nebulized anti-inflammatory medications. Furthermore, spacers can become plugged, torn, broken, or misplaced or can be left at home.

Future studies need to evaluate the use of these devices in younger children, especially in areas where neither spacers nor nebulizers are readily available.[1] This study shows that homemade spacers work in the hospital setting, but will they also work in the home setting? Will differences in priming and washing alter drug delivery?

It is worthy of note that to craft a spacer from a sealed cold drink bottled necessitated using a heated wire, as described in the original article by Zar and colleagues.

1 Pedersen S, Mortensen S. Use of different inhalation devices in children. *Lung* 1990;168(suppl):653-657.

Toolbox

Secondary prevention of transient ischemic attack and stroke

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Competing interests: None declared

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Stroke or transient ischemic attack is common and likely to be fatal or cause serious disability. A second stroke will not necessarily be of the same type as the initial event, although hemorrhages tend to recur (table 1). Patients with previous stroke commonly succumb to other vascular events, in particular myocardial infarction. Effective secondary prevention depends on giving attention to all modifiable risk factors for stroke and treating the causes of the initial stroke. Four questions should be answered:

IS IT ACUTE CEREBROVASCULAR DISEASE?

The key features of acute cerebrovascular disease are focal neurologic deficit, sudden onset, and the absence of an alternative explanation. An abrupt onset of a dense hemiparesis before gradual improvement in a conscious patient rarely causes doubt, but conditions that commonly mimic stroke must be considered (see previous article in *West J Med* 2000;173:209-212).

Table 1 *Risk of recurrence after stroke or transient ischemic attack*

Event	Risk of stroke
Stroke	8% a year
Transient ischemic attack	8% in first month 5% a year thereafter 5% a year*

*Risk of myocardial infarction.

Modifiable risk factors for stroke

- Hypertension
- Smoking
- Diabetes mellitus
- Diet: high salt and fats, low potassium and vitamins
- Excess alcohol intake
- Morbid obesity
- Little physical exercise
- Low temperature
- Cholesterol concentration—at least in patients with coronary disease

Embolic causes of stroke found on echocardiography

- Mitral stenosis
- Left atrial enlargement (>4 cm)
- Dyskinetic or akinetic left ventricle
- Severe global left ventricular dysfunction
- Valvular vegetation
- Left atrial or ventricular thrombus
- Mitral valve calcification
- Calcific aortic valves or stenosis predispose to embolism but may not justify anticoagulation

IS IT ISCHEMIC OR HEMORRHAGIC STROKE?

Neither clinical history nor examination can reliably distinguish infarction from primary intracerebral hemorrhage. A small hemorrhage can produce transient symptoms, although these rarely resolve within an hour.

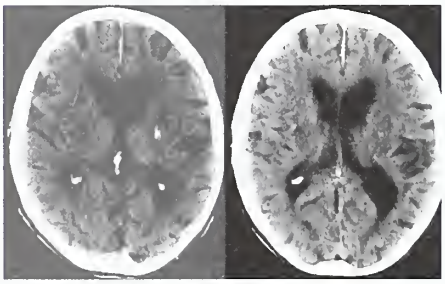

Figure 1 Computed tomograms on days 0 (left) and 8 (right) after left subcortical hemorrhage presenting as a transient ischemic attack with symptoms lasting 50 minutes. Note the resolution of diagnostic appearance at day 8.

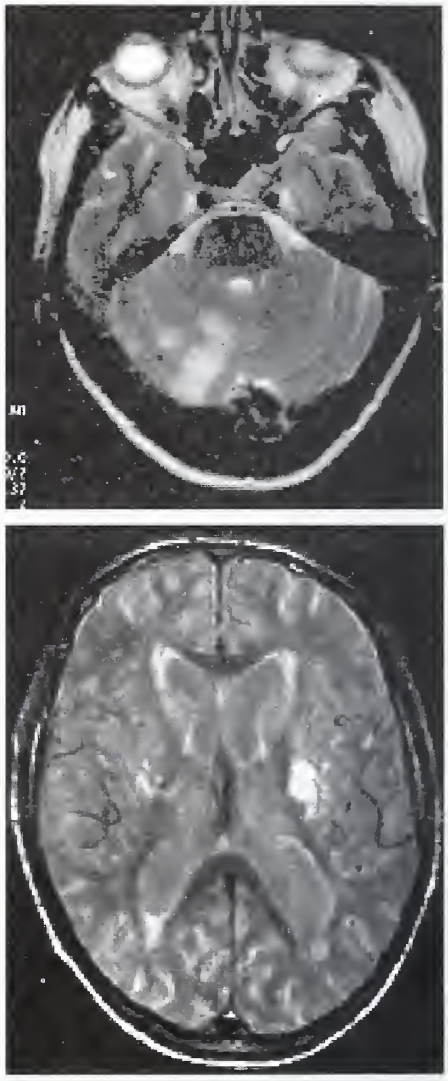

Figure 2 (top) Magnetic resonance image (MRI) of posterior fossa of brain in patient with right cerebellar infarction. (bottom) A T1-weighted MRI of left subcortical hemorrhage (day 9 in patient in figure 1).

Cerebral imaging is essential, and the choice and timing of the scan are important (figure 1). Hemorrhage is immediately apparent on computed tomography, but its distinctive appearance becomes indistinguishable from infarction over a few weeks; for major symptoms, a computed tomogram

Table 2 *Suggested imaging approaches for patients with symptoms of stroke*

Symptoms	<1 hr*	Duration 1 hr; onset <2 wk	>1 hr; onset >2 wk
Abrupt onset, typical cerebrovascular symptoms	Image only if anticoagulation proposed	CT	MRI
Insidious onset, possibly tumor	NA	CT with contrast	CT with constrast
Insidious onset, suggests multiple sclerosis	NA	MRI	MRI

CT = computed tomography; MRI = magnetic resonance imaging; NA = not applicable.
*A shorter interval may be applied depending on available resources.

taken within 2 weeks should still be diagnostic (table 2), but a small hemorrhage may be missed after 1 week.

Magnetic resonance imaging has a greater sensitivity than computed tomography for brain stem, cerebellar, and small ischemic strokes of the brain. It can also identify hemorrhagic stroke and remains diagnostic long after signs have become undetectable on computed tomography (figure 2).

IS THE CAUSE CARDIOEMBOLIC OR VASCULAR?

As many as a quarter of ischemic strokes are caused by embolism from the heart or major vessels. In these patients, full anticoagulation should be considered. Embolic stroke can affect any vascular territory but can rarely be diagnosed conclusively. Certain features should prompt a search for an embolic source. Transthoracic echocardiography is usually adequate, but transesophageal echocardiography is justified if the results are equivocal or the index of suspicion is high.

IS THE ANTERIOR OR THE POSTERIOR CIRCULATION INVOLVED?

The vertebrobasilar arteries supply the brain stem, cerebellum, and occipital lobes; the cerebral hemispheres are supplied through the carotid arteries. This distinction is important because carotid Doppler ultrasonography with a view to endarterectomy is justified in patients with severe carotid disease only if symptoms have arisen from the anterior circulation (figure 3).

HOSPITAL REFERRAL

Although the approach to the investigation of stroke is simple, few general practitioners will have access to the necessary facilities or see enough cases to develop expertise in interpreting the results. Patients with possible stroke need urgent telephone or fax referral to a "fast track" specialist cerebrovascular clinic or stroke unit because of the time limitations on the diagnostic capability

Justifications for echocardiography

- Atrial fibrillation
- Heart failure
- Myocardial infarction within 3 months
- Electrocardiographic abnormalities:
  Myocardial infarction or ischemia
  Bundle branch block
- Cardiac murmur
- Peripheral embolism
- Clinical events in ≥2 areas:
  Right and left hemisphere
  Anterior and posterior circulation
- ≥2 cortical events (even in same area) unless severe ipsilateral carotid disease

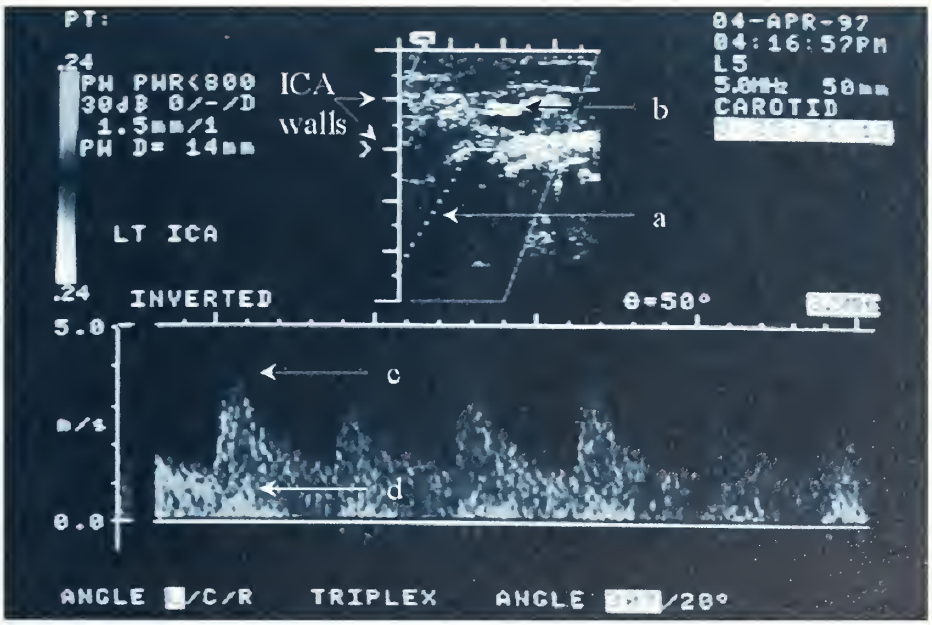

Figure 3 Carotid Doppler ultrasonogram in patient with severe internal carotid artery stenosis. The top panel shows the angle of insonation (a) of the internal carotid artery and sampling window (b); the velocity of systolic blood flow at the point of maximal narrowing (c) is nearly 4 m/s (normal <1 m/s). Stenosis causes flow velocity to increase and produces turbulence, which is seen as shading within the Doppler spectrum (d).

Table 3 *Complex cases that may require hospital referral*

Case	Possible treatment
Recurrent stroke or transient ischemic attack despite antiplatelet treatment (treatment failure)	Consider higher doses of aspirin, addition of dipyridamole (if not already prescribed), substitution or addition of clopidogrel, or substitution or addition of warfarin sodium
Recurrent embolic events despite adequate anticoagulation with warfarin	Consider adding low dose-aspirin
Recurrent nonhemodynamic symptoms from inoperable severe carotid stenosis or serious intracranial stenosis despite anitplatelet treatment	Consider warfarin
Hypertension and inoperable severe carotid stenosis	Consider cerebral blood flow monitoring (with ultrasonography or radionucleotide perfusion scanning) before antihypertensive treatment

of computed tomography and the limited availability of magnetic resonance imaging (table 3).

MANAGEMENT OF RISK FACTORS

Smoking is an important correctable risk factor and should be strongly discouraged. The risk of stroke in a smoker returns to that of a nonsmoker within 3 to 5 years after stopping smoking.

The immediate reduction of blood pressure may be deleterious, but long-term risk is inversely related to the blood pressure achieved (table 4). Treatment may, therefore, be justified even in patients with "normal" blood pressures. Hypertension should be treated 1 to 2 weeks after a stroke according to the British Hypertension Society guidelines (figure 4). Patients at high risk of a further stroke (such as elderly people) derive the greatest benefit from treatment.

The role of serum cholesterol concentration in the pathogenesis of stroke remains debatable. Nevertheless, HMG CoA reductase inhibitors (statins) have been shown to reduce the risk of stroke in clinical trials of patients with coronary artery disease. Lowering cholesterol concentrations with a statin after atherosclerotic stroke or transient ischemic attack probably reduces recurrent events and the risk of ischemic heart disease developing. Because stroke patients represent a high-risk group, the cost of treatment may be justified.

Diabetes confers a substantial disadvantage for survival and functional outcome on patients with acute stroke. The mechanism for this is unknown, but because it is a long-term effect, attempts should be made to normalize blood glucose concentrations. Blood pressure targets are lower for diabetic than nondiabetic patients.

Elevated plasma homocysteine concentration is increasingly linked to premature vascular disease, and it can be easily lowered through vitamin supplements (folate and pyridoxine). Although the value of lowering homocysteine concentrations has not been proved, younger patients with raised plasma homocysteine concentrations may benefit from supplementation.

ANTIPLATELET THERAPY AND ANTICOAGULATION

Patients with atrial fibrillation should receive warfarin sodium if they have no contraindi-

Main contraindications to long-term warfarin sodium treatment

- Gastrointestinal bleeding
- Active peptic ulceration
- Frequent falls
- Alcohol misuse
- History of intracranial hemorrhage
- Age, by itself, is not a contraindication

Table 4 *Blood pressure (BP) targets (mm Hg) in nondiabetic and diabetic stroke patients*

BP target	No diabetes	Diabetes
Titrate to diastolic	≤85	≤80
Optimal	<140/85	<130/80
Suboptimal	≥150/90	≥140/85

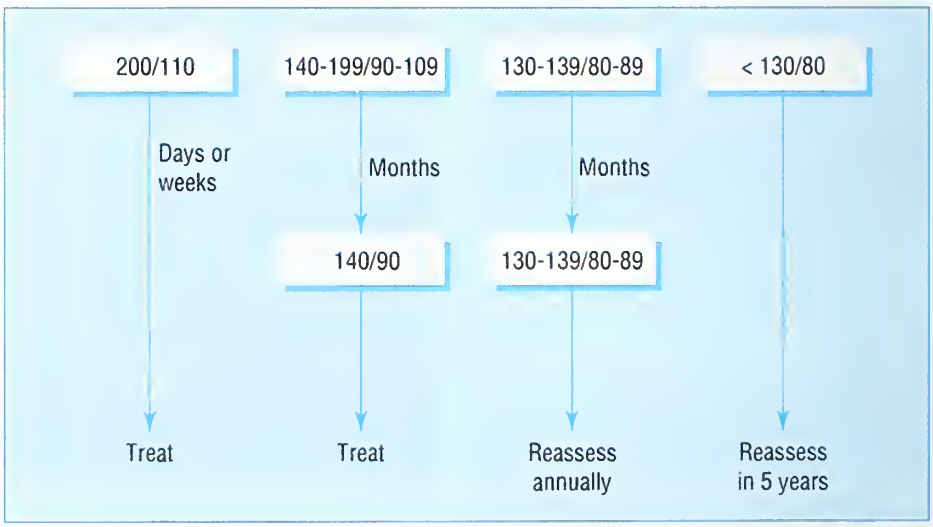

Figure 4 Blood pressure thresholds (mm Hg) for treatment after stroke or transient ischemic attack (based on British Hypertension Society guidelines 1999).

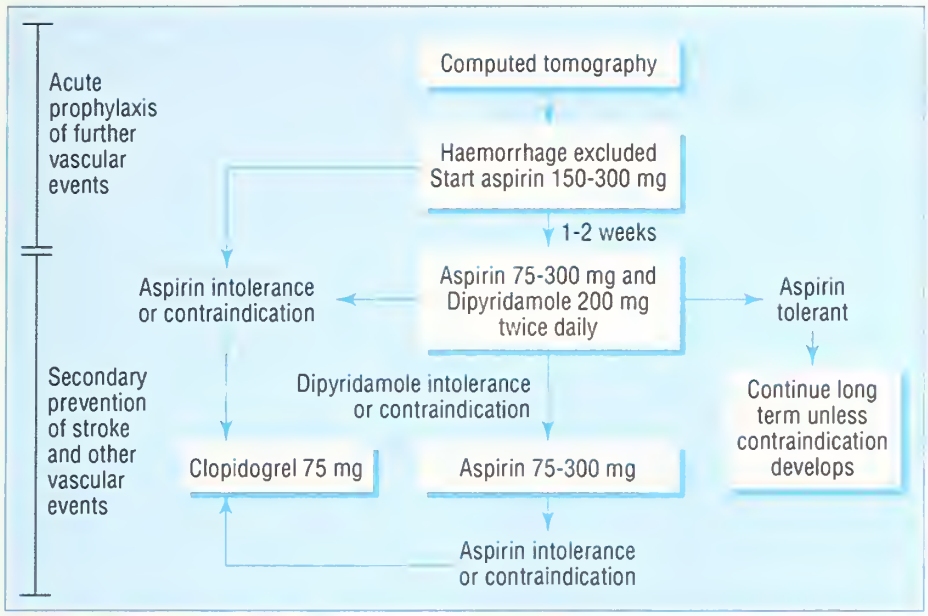

Figure 5 Aspirin as the first line of antiplatelet therapy after stroke

cations, aiming at an international normalized ratio of 2.0 to 3.0. Patients with other important sources of cardiac embolism also benefit from warfarin therapy. Only patients with mechanical prosthetic heart valves require a higher target international normalized ratio of 2.5 to 4.5, although the exact value depends on the type of valve.

For all other patients with ischemic stroke, antiplatelet therapy would be first-line treatment (figure 5). Aspirin is inexpensive and simple to administer, and its benefits are conclusively proved. An initial dose of 300 mg, followed by 75 mg daily, is advised (higher doses have little advantage but increase gastrointestinal side effects and the incidence of bleeding).

Modified-release dipyridamole (200 mg twice a day) has an independent and additive effect to low-dose aspirin therapy in preventing further strokes but not coronary events or overall mortality. The routine addition of dipyridamole to the use of aspirin for secondary prevention of strokes may be cost-effective.

Clopidogrel (75 mg daily), a new antiplatelet drug, is well tolerated and was slightly more effective than aspirin in a large trial. However, it is not cost-effective for initial treatment. Clopidogrel should be used in patients with true intolerance to aspirin (allergy or intractable side effects with low-dose enteric-coated aspirin with or without the use of antiulcer drugs); dipyridamole alone does not prevent cardiac events.

Indications for carotid endarterectomy

Surgery not indicated

- Carotid area symptoms and ipsilateral stenosis of 0% to 69%
- Complete occlusion of the carotid artery

Surgery indicated

- Carotid area symptoms within 6 months and ipsilateral stenosis of 70% to 99%
- Carotid area symptoms within 12 months and ipsilateral stenosis of 80% to 99%

CAROTID SURGERY AND ANGIOPLASTY

Firm evidence from 2 large trials has clarified the role of carotid endarterectomy in patients with ipsilateral severe carotid stenosis (figure 6). Patients with severe disease benefit from surgery for as long as 12 months after the most recent cerebral event. The benefit derived is inextricably linked to the operative risk (stroke or death within 30 days)(figure 7). In randomized trials, the operative mortality in patients with severe disease was

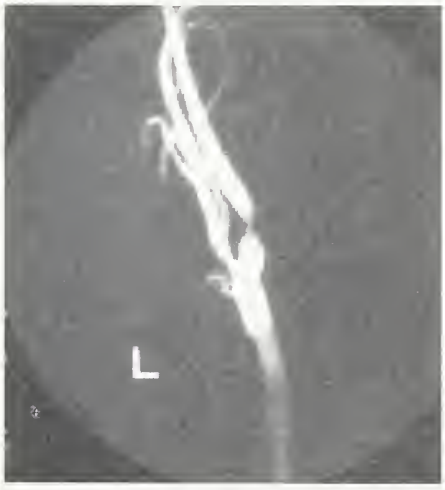

Figure 6 Angiogram showing tight stenosis of internal carotid artery just distal to the bifurcation

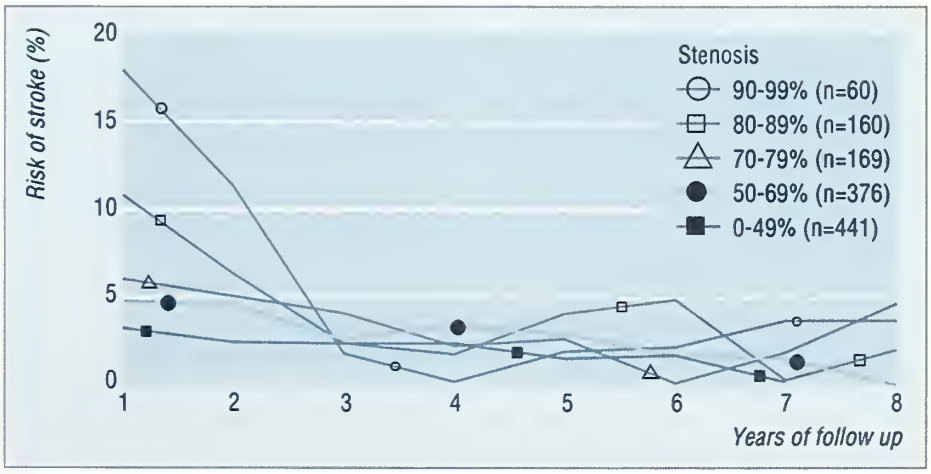

Figure 7 Risk of stroke in patients not having surgery according to degree of stenosis. Data from the European Carotid Surgery Trial (*Lancet* 1998;351:1379-1387).

Table 5 *Summary of results from European Carotid Surgery Trial*

Stenosis, %	Incidence of stroke, % Surgery arm	Medical arm	Absolute risk reduction, %	Relative risk reduction, %
0-30	11.8	6.2	−5.6 at 3 yr	None
31-69	16.0	15.0	−1.0 at 5 yr	None
70-99	12.3	21.9	9.6 at 3 yr	44 at 3 yr

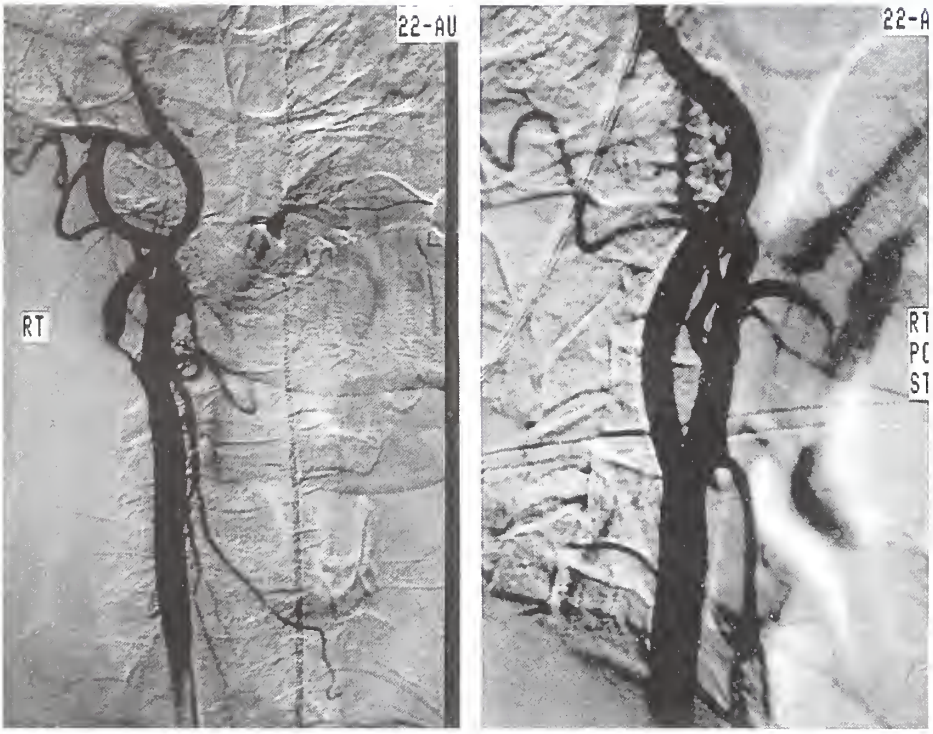

Figure 8 Severe carotid stenosis before (left) and after carotid angioplasty and stenting (right)

1.0%, the risk of death or disabling stroke less than 4.0%, and the risk of death or of any stroke less than 7.5% (table 5). Surgical risk is inversely proportional to surgical volume, implying that patients should be referred to busy carotid endarterectomy centers. Surgeons must quote their own risks rather than results obtained in trials.

Any patient presenting with carotid area symptoms should be considered a possible candidate for carotid endarterectomy, and carotid Doppler ultrasonography should be done if the patient is fit for surgery. The presence or absence of a carotid bruit is irrelevant. An ongoing meta-analysis may further refine the indications, particularly regarding the management of women and patients with isolated retinal symptoms, who seem to have a lower overall risk of stroke.

A successful carotid endarterectomy is not a major procedure, and most patients can be discharged home the day after surgery. Neither clinical nor ultrasonographic surveillance prevents late stroke, and so most patients are discharged from follow-up at 6 weeks with the proviso that they should be referred immediately should further cerebral ischemic events occur.

In carotid angioplasty, the stenotic area is dilated by using a balloon catheter introduced percutaneously through the femoral artery (figure 8). The potential advantages of carotid angioplasty include reduced hospital stay and incidences of cranial nerve injury, wound complications, and other cardiovascular morbidity. The main concern about carotid angioplasty is the risk of embolic stroke at the time of the procedure and recurrent stenosis. Carotid angioplasty aids the management of fibromuscular dysplasia, radiation injury, and symptomatic restenosis after carotid endarterectomy. Otherwise, carotid angioplasty should not be performed outside randomized trials, and as with carotid endarterectomy, outcomes in individual centers should be audited.

COMPLEX CASES

Secondary prevention of stroke is rightly the province of general practitioners, and the preceding suggestions concern most patients with recent stroke. However, patients with complex conditions need specialist services, although definitive trial evidence justifying therapeutic decisions in such patients is often absent. Patients should be monitored for compliance with treatment and the development of complications such as renovascular disease, ischemic heart disease, and further cerebrovascular problems. Optimal dietary, smoking, lipid, and blood pressure management is always required in addition to antithrombotic treatment.

G T McInnes and L Ramsay contributed toward the blood pressure guidelines. M R Walters supplied some of the pictures, and J Overell supplied the antiplatelet flow chart.

Further reading

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Best Practice

EVIDENCE-BASED CASE REVIEW

Treating hypertension

CASE HISTORY

The patient, a 66-year-old retired bar owner, Mr C, was admitted to the hospital with a sudden onset of weakness affecting his right arm and right leg. His wife had been unable to get him out of bed earlier that morning. She had noted that his speech was slurred and initially had thought that he was very confused. The day before, he had knocked his head against a car door but had seemed all right at the time. He had no history of transient ischemic attacks. A diagnosis of essential hypertension had been made 4 years previously, and angina pectoris had been diagnosed 2 years previously. Although his general practitioner had prescribed antihypertensive treatment, Mr C did not like the side effects of the drug and stopped taking it 3½ years ago. His only other medication was sublingual glyceryl trinitrate (nitroglycerin) as required. He smoked 20 cigarettes a day, having started at age 20, and consumed 40 units of alcohol per week. Mr C's father had died of a myocardial infarction at age 69, and his mother had died of a stroke at age 70. He had no siblings.

Physical examination revealed his power to be reduced at 3/5 in his right arm and right leg, and he had an expressive dysphasia. Tone was increased on the right, with a right extensor plantar response, and he had hyperreflexia on the right compared with the left. He was continent and had fair sitting balance.

A 12-lead electrocardiogram confirmed that Mr C was in sinus rhythm with left ventricular hypertrophy and an old inferior myocardial infarction. His full blood cell count, erythrocyte sedimentation rate, random blood glucose concentration, and levels of troponin T, urea, creatinine, and electrolytes were all within the normal range. A fasting lipid profile revealed a cholesterol concentration of 7.2 mmol/L (278 mg/dL). A computed tomographic scan of the brain showed a cerebral infarct in the internal capsule. Doppler studies showed no significant stenosis of the carotid arteries. Echocardiography showed good left ventricular function with an ejection fraction of 59% and mild mitral regurgitation. After rehabilitation, Mr C was discharged home, independently mobile with a walker.

When the patient was seen in the outpatient clinic 8 weeks later, his primary care physician had sent a letter expressing concern at Mr C's continued raised blood pressure, which in the clinic was 182/102 mm Hg sitting. On further inquiry, the patient indicated that although he had been discharged home with the medications aspirin, pravastatin, and atenolol, he had taken only aspirin after discharge. He had not had any adverse effects from the drugs but was reluctant to take any medication and wanted to know exactly what evidence existed that he would benefit from taking regular antihypertensive medication, especially because he was totally free of symptoms.

Summary points

- Reduction of diastolic blood pressure by 5 to 6 mm Hg reduces the risk of stroke by 42% in hypertensive patients
- The same reduction in diastolic blood pressure reduces the risk of coronary heart disease by 14%
- Most of the randomized controlled trials have used either β blockers or diuretics as the antihypertensive agent
- Diuretics (thiazides) seem to be superior to β blockers in reducing the risk of stroke

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Competing interests: None declared

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WHAT IS THE EVIDENCE FOR TREATING ONGOING HYPERTENSION IN PATIENTS WHO HAVE HAD A STROKE?

Searching for the evidence

With increasing access to the Internet and articles on health in popular media, patients are becoming more knowledgeable about their illnesses, and some want to discuss with their physician the information they obtain from these sources. For physicians to keep abreast of every new development in every field of medicine is impossible, but it is important that they develop skills in seeking new information that they can assess and use to make informed decisions.

Mr C's risk factors for stroke

- Age
- Hypertension
- Ischemic heart disease
- Hyperlipidemia
- Smoking
- Heavy alcohol consumption

Mr C wants to know what evidence exists that would support his taking antihypertensive and lipid-lowering drugs. Although most of the standard medical textbooks clearly state that hypertension is a risk factor for stroke (see box) and should be treated, few quote the exact evidence on which this conclusion is based.

The ideal evidence to convince Mr C to take antihypertensive drugs would be large randomized controlled trials showing a substantial benefit in patients who received treatment. One of the easiest and most readily available sources to start with is MEDLINE. First, I need to decide which words to use in my search and how far back to extend the search. Although initially I was going to use "hypertension" and "stroke," by consulting MEDLINE's thesaurus, I learn that "cerebrovascular disorders" is a better term to use than "stroke." I decide to go back as far as 1990 for the search.

Appraising the evidence

When I use the terms "hypertension" and "cerebrovascular disorders," MEDLINE provides 970 records, but when I limit the search to randomized controlled trials and only those in the English language, it gives 43 references. Although it might be possible to restrict the search further, I prefer to print out the references and look at the title of the study and the journal in which the study was published. By doing this, I was able to select 3 references that may answer Mr C's question.[1-3]

Summarizing the evidence

Fortunately, someone has already done an overview of 14 randomized controlled trials of blood pressure, stroke, and coronary heart disease.[1] These trials involve a total of 37,000 people randomly allocated to antihypertensive treatment (mainly diuretics or β blockers), with a mean treatment duration of 5 years. For most of these trials, a cutoff blood pressure of 140/90 mm Hg was used to determine hypertension. The results indicate that a decrease in the diastolic blood pressure of 5 to 6 mm Hg reduces the risk of stroke by 42% and coronary heart disease by 14%. The Systolic Hypertension in the Elderly Program,[2] in which 4,736 people from 447,921 screened participants aged 60 years and older were randomly allocated to either active or placebo treatment, showed that the treatment of isolated systolic hypertension in elderly people decreases their risk of stroke by 36%.

In another study, 4,396 patients aged 65 to 74 years with mild to moderate hypertension were randomly assigned to receive diuretic, β blocker, or placebo.[3] Patients in the treatment group had a 25% reduction in stroke and a 19% reduction in coronary artery events. In this study, supported by others,[4] diuretics seem to be superior to β blockers in reducing the risk of stroke in older people with hypertension. None of the trials included very elderly patients, as a consequence of which the question of whether they will benefit is somewhat uncertain (a trial is under way to answer this).[5]

CONCLUSION

Firm evidence exists that treating hypertension in persons at risk is beneficial and substantially reduces the risk of both stroke and, to a lesser extent, coronary heart disease. I relayed the information back to Mr C, who is now agreeable to taking his antihypertensive drugs. Given the findings on the electrocardiogram of an old myocardial infarction and his history of angina, I have decided to prescribe a β blocker. If these were absent, however, the available evidence would support the use of a thiazide diuretic as first-line treatment. If on subsequent review his blood pressure is not adequately controlled with a β blocker, I will add a thiazide diuretic.

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TOPIC IN REVIEW

Notifying survivors about sudden, unexpected deaths

This article is an edited version of a chapter in the book *Grave Words: Notifying Survivors About Sudden, Unexpected Deaths,* copyright 1999, by Kenneth V Iserson. Used with permission of Galen Press, Ltd (PO Box 64400, Tucson, AZ 85728-4400; phone: 1-800-442-5369 or 520-577-8363; fax: 520-529-6459; web site: http://www.galenpress.com), and Kenneth V Iserson. A teaching videotape, *The Gravest Words,* slide sets, and pocket-sized book of protocols are also available from the publisher. Prices and shipping details are on the web site.

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Summary points

- A sudden, unexpected death leaves survivors unprepared for their loss
- Physicians can learn effective techniques for notifying survivors about such a death
- It is important to use nonmedical language when preparing survivors for bad news
- What survivors want most is a notifier who seems to care that their loved one has died
- Notification protocols can help notifiers prepare for their task and help them understand what to expect

THE PROBLEM

Death has replaced sex as the major taboo topic in western culture. Imaginary death—such as the cartoonlike violence portrayed on television and in movies—has replaced reality for most people. When death strikes, as it must, and especially if it strikes suddenly and unexpectedly, we respond with discomfort, distress, and dismay.

A sudden death is one that is unforeseen, unexpected, occurs with little or no warning, and that leaves survivors unprepared for the loss. It comes from an unexpected injury or suicide or from a medical cause such as heart attack, stroke, overwhelming infection, poisoning, or massive bleeding. Death might even result from fear.[1,2] We have no ingrained cultural responses to tell us how to deal with these crises.

Survivors are victims. Their reactions separate them from life, from reality, and often from caring about themselves, their future, or those around them. When a person learns of the sudden unexpected death of a loved one (bereavement), they experience

> a sense of being lost and not knowing what to do. Their sense of being suspended from life, inability to concentrate, indifference to immediate needs, disbelief that the decedent is really gone, and feeling that life can never be worth living again hinders their ability to arrange for the funeral and to make plans for other ongoing life needs.[3]

This is grief.

No one likes to deliver the news of a sudden, unexpected death to others; it is an emotional blow, precipitating life crises and forever altering their worlds. Yet, many health, law enforcement, religious, and social service professionals must repeatedly do this as part of their daily work. It can be an emotionally draining and even harrowing experience. This article is designed to help us perform these duties with more skill, aplomb, and assurance.

Perceptive survivors can easily tell which notifiers care and which are only "going through the motions." It often takes imagination to put oneself in the position of a grieving survivor, especially when wide cultural or age differences exist. Imagination, studying people, advance planning, and learning from experienced mentors is the only way to successfully perform this necessary but tragic task.

Even if you cannot learn to empathize with survivors whose life experience may differ considerably from yours, you can learn to behave appropriately, speak correctly, and assist them in their time of grief. Using death-notification protocols and being accompanied by more experienced partners may be the only way to positively affect these survivors.

WHY SUDDEN, UNEXPECTED DEATH NOTIFICATION IS UNIQUE

Sudden, unexpected deaths severely shock survivors. These deaths strike blows to the very essence of life for those left behind. The decedent's sudden transition from being alive to being dead shocks all observers, both professionals and lay people alike. The degree of this shock is related to how independent, autonomous, and distinctive the decedent was when he or she died.[4]

Some sudden deaths can even be considered calamitous when victims die unexpectedly of violent, destructive, demeaning, or degrading causes such as murder or suicide. These deaths can profoundly affect the victim's community, some deaths more than others.[4]

Once a person is dead, the survivors become the victims, the patients—those in need. Sudden deaths often represent major life transitions for the survivors. In an

instant and with no warning, women go from being wives to being widows, children become orphans, and friends survive alone.

In modern societies, people often do not witness the events that bring them grief. Survivors need someone to communicate this news to them. So the primary role of the death notifier is to "break the bad news."

A word must be said here about the commonly used terms, "breaking or delivering bad news." As death educator Kyle Nash says (written communication, April 1999),

> These negatively value-laden phrases imply one-sided communication, which should never be the goal of any notifier-survivor relationship. If the communication is thought of in that manner at the outset, notifiers will tend to feel awkward, anxious, and uncomfortable about what they will be or are communicating. When notifiers feel uncomfortable, the type of communication that occurs in these situations does become one-sided.
>
> While it may seem obvious that death notification will indeed be interpreted as negative (that is, bad), I believe that only the survivors can determine what the information means to them. Preferable terms that I use when teaching are "initiating or engaging in difficult conversations." These phrases clearly express 2-way communication and are value neutral.

Survivors' first reaction when they hear the news is often, "It can't be true! It can't be happening!" The professionals around them must give all the support that they can to allow this unfortunate truth to sink in. Family members of those who die suddenly and unexpectedly, either in an emergency department or in a hospital (and also presumably outside the hospital) do much more poorly than those whose deaths are expected. This may be because there is no time for psychological preparation.[5-7]

EXPECTED VERSUS SUDDEN, UNEXPECTED DEATHS

Most people's deaths can be anticipated. Those who die are usually elderly people with chronic, often obviously progressive, diseases. Even if the exact day, week, or even month when the death occurs comes as a surprise, no one is surprised when it happens. The differences between these expected deaths and sudden unexpected deaths are illustrated in the table on p 263.

WHO ARE THE NOTIFIERS?

In the United States and Canada, about 70% of deaths occur in health care institutions, so their staff is usually responsible for notifying survivors about the death. In the other 30%, however, this job falls to the police, ambulance or fire department personnel, chaplains, medical examiners or coroners, or coworkers. In nearly all cases, regardless of whether the death occurs in a health care facility, family members and friends of the decedent must then notify others.

NOTIFICATION OF A DEATH DURING A RESUSCITATION ATTEMPT

Importance of nonmedical language

Within most medical facilities, protocols determine who is considered to be the notifier. If a family arrives at the hospital while resuscitation attempts are ongoing, a chaplain, social worker, or nurse may be delegated to inform the family of the patient's status. These professionals may be more inclined to use nonmedical words to explain what is occurring than would a physician. This is vital because, despite its wide use in the media, the jargon commonly used in hospitals is unfamiliar to most people. To avoid any miscommunication, health care workers who act as notifiers should use "heart attack" rather than "MI," "injury" rather than "trauma," and "breathing machine" rather than "ventilator."

Updating the family

These notifiers should continually update the family about any changes. When things are going badly, the same person, or at least 1 person from the group who initially spoke with them, should progressively inform the family that "things are not looking good." This alerts them to the grave situation and gives them at least a little time to prepare for the bad news. This psychological preparation for the loss of their loved one is often disparagingly termed "hanging crepe," but survivors usually view it as "being gentle." Technically, the strategy is called "presaging" or allowing survivors time for "anticipatory grief." Some have also referred to these updates as "successive preannouncements" and "preliminary suspicion announcements," sug-

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Expected versus sudden, unexpected deaths

Characteristic	Sudden, unexpected death	Expected death
Approach of death	Immediate or in a short time	Gradual
Nature of illness or injury	Acute process or acute worsening of a stable chronic illness	Chronic—usually an illness or combination of illnesses
Causes of death	Disease, suicide, homicide, accidental, disaster, or unknown cause	Usually disease or a result of aging processes
Age of decedent	Any age, commonly young or middle-aged adults, fetuses, and neonates	Usually elderly but can occur at any age
Place of death	Usually in public, emergency department intensive care unit, or at home or work	Usually home, hospital, or nursing home
When death occurs	At the time of or shortly after the acute event	Months to decades after diagnosis of chronic disease occurring in old age
Survivor reaction	Disbelief, shock, grief, dismay, disorganization, hostility, and fear	Grief
Survivor involvement	Usually not present at death; appear gradually at death scene or emergency department	Often present at death or aware of impending death
Site of last contact with medical personnel	Public space, home, or emergency department	Hospital, home, hospice, or nursing home
Resuscitation procedures	Often performed	Rarely performed; advance directives often available
Patient identity	Known or often, at least initially, unknown	Usually known
Autopsy	Frequent and done by medical examiner or coroner	Rare, and when done, usually by hospital pathologist
Family's immediate after-death rituals and requirements	Usually not prearranged	Often prearranged by dying person or family in anticipation of death

gesting that it is a gradual build up to what is expected to be tragic news.[8]

In a typical emergency department scenario, a nurse, chaplain, or social worker acts as the liaison between the resuscitation team and the family. They meet family members as they arrive and guide them to a waiting area. Having already been in the resuscitation room, the liaisons have a sense of or have been explicitly told about the patient's condition and what chance the clinicians think the patient has of making it out of the emergency department and the hospital alive and functional. They in turn deliver this news to the family. Initially, they may say, "The medical [surgical] team is working very hard, but he is very ill [badly hurt]." On subsequent visits, they will reassure the family that the team is still working but will say "Things are not looking good" or "They are not sure they will be able to save him." Ultimately someone, usually the physician in charge, will tell the family that the effort was unsuccessful. By that time, it is news they have been prepared to hear.

WHAT SHOULD PHYSICIANS DO?

In some instances, the physicians or surgeons only need to stop, shake their heads, and say "I'm sorry" for survivors to get the news they expect. In these cases, the physicians clearly mean they are sorry for the survivors' loss as well as for their own inability to change the outcome. It is hoped that after delivering the news in this way, they take the time to sit with and assist the survivors for at least a short time. When these nonverbal or minimally verbal announcements fail, clinicians must fall back on their standard death notification methods.

Occasionally, interactions between the clinician and survivors during resuscitation attempts convey important clinical information. As Dr Bob Orr relates (oral communication, March 1999):

> Things weren't going well during an emergency department resuscitation and I had "hung crepe" a few times with the potential widow. Finally, I told her that we were only continuing with CPR because his pupils had not

Box 1
Telling survivors about sudden unexpected deaths may be difficult for physicians because they often

- Lack training and experience
- Fear being blamed
- Do not know how to cope with survivors' reactions
- Fear expressing their emotions
- Fear not knowing the "right" answers
- Fear their own death or disabilities

dilated, so that we thought his brain might still have some function. "But he has 2 glass eyes," she said. We stopped.

THE NOTIFICATION OF DEATH

Once death has occurred, especially in an emergency department, the physician usually has the task of delivering the news, often accompanied by a chaplain, a nurse, or a social worker. Most survivors have no objection if more timely notifications can be made by other professionals, such as a nurse, chaplain, or social worker, as long as they have subsequent contact with the physician.[5] What survivors want most is a notifier who seems to care that their loved one has died—someone who will inform them in a warm, sympathetic tone of voice. As a survivor who did not have that experience said: "I could not believe that a death that was so important to me was so unimportant to the people in that emergency room. I left thinking that there must be something wrong with me, that somehow I should not be feeling the way I was feeling. I felt as though I was abnormal."[9]

Some professionals avoid this responsibility and pass the job to others. This is usually because they have difficulty dealing with one or more aspects of death or the interaction with survivors. This task, however, should never be relegated to the unit assistant, medical or nursing student, or other untrained or partially trained person. The exception to this is when a student or resident, who is in the process of being educated to the death-notification process, is accompanied by an experienced, supervising mentor.

When reluctant notifiers must speak with survivors, they often use a standard, rapid, unconcerned approach as a defense. Others, even those who try to do a good job, just "wing it," using whatever method seems best. For professionals, these can be career-crippling strategies.

Box 2

This is a survivor's description of a home notification she endured. It has been modified and used with permission.[13] The survivor was woken in the night by a police officer and a chaplain, who began to ask her questions:

"You start wondering who is in trouble. Your mind begins to race down the checklist of family members: your husband is at work; your son has been staying out too late recently; your daughter is expecting her first child, and she and her husband have been arguing a lot recently.

As this stranger, these 'intruders,' continues asking questions, your own questions start flashing though your mind. Your world begins crumbling in on you. You are brought back to the present moment by an insistent voice gently but firmly calling your name. 'Are you all right?' You look at the speaker's face, trying to read what is being said. You hear your own voice, as from a distant point saying, 'Yes, I'm all right.' Those probing, insistent voices then ask, 'Is your husband at home?' You feel yourself beginning to feel faint. The voices urge you to go inside and sit down. As you sit, they ask about your husband again. You take a deep breath, trying to clear some of the cobwebs from your thoughts. Finally, you realize your husband is at home. He traded nights off with a friend and is sleeping. You call him several times before he answers, and you ask him to come downstairs.

Taking the stairs 2 at a time, he hurries to your side. 'Who are you?' he asks them, as he puts his arm protectively around your shoulder. You introduce your husband to these strangers who are obviously bringing bad news, although they radiate a calmness and a genuine friendliness that help you feel a little less anxious. Icy fingers of fear clutch your throat as you hear the question, 'Do you have a son named Tom? He has wavy blond hair and a moustache?' Your hands move to your throat as though to seek release from that stranglehold of fear. The questions continue. 'Is your son about 18 years old? Does he drive a blue antique pickup truck?'

Almost at the same instant as you say 'Yes,' the pent-up fear erupts as you cry out in anguish, 'Oh my God, what has happened?' It seems an eternity before you hear those dreaded, but not unexpected words, 'I'm sorry, your son has been involved in an accident.' The words, even though spoken softly and compassionately, shatter your world. Though dazed by this news, you feel compelled to strike out against its reality. With your heart pounding and aching, blinded by the tears that gush uncontrollably from your eyes, you jump up from the chair to vent your anguish by beating on these people who have torn your little world asunder. Your husband, stunned by the news, now moves to your side. One of the intruders gently but firmly has been holding your wrists, saying, 'It's all right, go ahead and vent your anger and hurt.' You feel your husband's arm around you, and he leads you back to your chair. As you sit, your husband asks, 'How bad is it? Is he hurt bad?' 'Yes,' comes the reply, 'it is very serious.' Looking at the intruders and wanting them to deny the next question, you and your husband ask in a single voice, 'Is he . . . dead?' Stepping closer to where they can touch both of your shoulders, the intruders answer very softly, 'Yes.'

The dam of restraint can no longer hold back the deluge of tear-filled anguish. The intruders silently, and understandingly, wait with patience until the sobbing subsides. After a while, you and your husband look at them as sources of guidance, strength, and information. You ask 'What happened?' The intruders, now companions in this sorrow, review the incident with sufficient detail for you to understand what happened. They answer, to your satisfaction, the questions of who was involved, where it happened, how it happened, and where your son's body is now. They ask if they can contact your own clergy. As you look at your husband, he nods his head and says, 'Yes, we would appreciate that.' "

A key psychological response that often diminishes notifiers' effectiveness is identifying too closely with survivors, thus becoming entangled in their emotions. This may be due to the notifier having experienced a similar event or closely matching the key survivor's age, cultural background, and social or professional position. There are several reasons why it may be difficult for physicians to tell survivors about sudden unexpected deaths, as shown in box 1.[10]

The qualities of a good communicator are genuineness, warmth and respect for the survivors, active listening, empathy, and openness.

WHY USE PROTOCOLS?

It has been claimed that "effective grief support cannot be reduced simply to a protocol-driven response."[11] It is true that no protocol can anticipate every eventuality; every notification will differ in some way. Neither can it enable notifiers to break bad news painlessly. It can, however, help notifiers prepare for their task and help them understand what to expect. Protocols combined with staff education have made significant differences in how survivors perceive and respond to sudden-death notifications.[12]

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CLINICAL EVIDENCE

Bell's palsy

This article comes from *Clinical Evidence* (2000;3:573-576), a new resource for clinicians produced by the BMJ Publishing Group. *Clinical Evidence* is an extensively peer-reviewed publication that summarizes the best available evidence on the effects of common clinical interventions gleaned from thorough searches and appraisal of the world literature. It became available in the United States late last year. Please see advertisement for more information or, alternatively, visit the web site at www.evidence.org.

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QUESTIONS: What are the effects of medical treatment of Bell's palsy in adults and children? How effective is steroid therapy? How effective is antiviral therapy?

DEFINITION

Bell's palsy is an acute, unilateral paresis or paralysis of the face in a pattern consistent with peripheral nerve dysfunction, without detectable causes.[1] Additional symptoms may include pain in or behind the ear, numbness in the affected side of the face, hyperacusis, and disturbed taste on the ipsilateral anterior part of the tongue.[2-5]

INCIDENCE/PREVALENCE

The incidence is around 23 per 100,000 people per year, or about 1 in 60 to 70 people in a lifetime.[6] It affects men and women more or less equally, with a peak incidence between the ages of 10 and 40. It occurs with equal frequency on the right and left sides of the face.[7]

ETIOLOGY AND RISK FACTORS

The cause is unclear. Viral infection, vascular ischemia, autoimmune inflammatory disorders, and heredity have been proposed as the underlying cause.[2,8,9] A viral cause has gained popularity since the isolation of the herpes simplex virus-1 genome from facial nerve endoneurial fluid in people with Bell's palsy.[10]

PROGNOSIS

More than two thirds of people with Bell's palsy achieve full spontaneous recovery. The largest series of people with Bell's palsy who received no specific treatment (n = 1,011) found the first signs of improvement within 3 weeks of onset in 85% of people.[11] For the other 15%, some improvement occurred 3 to 6 months later. The same series found that 71% of people recovered normal function of the face, 13% had insignificant sequelae, and the remaining 16% had permanently diminished function, with contracture and synkinesis (involuntary movement accompanying a voluntary movement). These figures are roughly similar to those of other series of people receiving no specific therapy for Bell's palsy.[7,8,12]

Summary points

- A systematic review of randomized controlled trials (RCTs) has found no good evidence that steroids provide long-term benefit
- One RCT found that prednisone was better than acyclovir in improving recovery of facial motor function
- One RCT found that acyclovir was better than placebo in people receiving prednisone

AIMS

To maximize recovery of facial function and to reduce the risk of sequelae, with minimal adverse effects.

OUTCOMES

The grade of recovery of motor function of the face, the presence of sequelae (synkinesis, autonomic dysfunction, and hemifacial spasm), and the time to full recovery.

METHODS

We did a *Clinical Evidence* search and appraisal in November 1999. All identified trials were reviewed. Trials used different scoring systems for reporting outcomes. Search date 1995; primary sources were MEDLINE, BIDS, Science Citation Index, and communication with manufacturers and specialists.

QUESTION: What are the effects of treatment in adults and children?

CORTICOSTEROIDS

A systematic review of randomized controlled trials (RCTs) has found no significant difference between ste-

roids and placebo either in the proportion of people achieving good recovery of facial motor function or in the proportion left with permanent sequelae. One poor-quality RCT found that steroids decreased the frequency of synkinesis and autonomic dysfunction.

Benefits

Versus placebo or no specific treatment: We found 1 systematic review (search date 1995, 4 RCTs, n = 390, 180 receiving steroids vs 210 controls).[13] Two of the trials were of good quality, and we found no subsequent RCTs of sufficient quality. The review found that steroids significantly improved the recovery of facial motor function. However, this conclusion was affected by the inclusion of an RCT in which 29% of participants were unavailable for follow-up.[14] If this trial was excluded, the result was no longer significant. Pooled results of the 2 high-quality RCTs (n = 75, both double-blind) found recovery of facial motor function in 25 of 38 people taking steroids and 25 of 37 controls (relative risk [RR] 0.97, 95% confidence interval [CI] 0.70-1.33). There was no significant difference in the time to recovery. **Versus acyclovir:** See discussion of antiviral treatment.

Harms

No serious adverse effects were reported in these trials.

ANTIVIRAL TREATMENT

One RCT found that in people receiving prednisone, the addition of acyclovir was better than that of placebo in improving recovery of facial motor function.

Benefits

We found no systematic review. **Versus placebo:** We found 2 RCTs.[15,16] The first enrolled 119 participants, of whom 20 (16%) were unavailable for follow-up, 53 received acyclovir (400 mg 5 times a day for 10 days), and 46 received placebo. All participants received prednisone. The proportion of people with good recovery of facial motor function was significantly higher in those receiving acyclovir and prednisone combined (49/53 vs 35/46, RR 1.22, 95% CI 1.02-1.45). The difference in the incidence of sequelae was nonsignificant, although there was a trend favoring those receiving acyclovir and prednisone (7/53 vs 13/46, RR 0.47, 95% CI 0.20-1.07).[15] The second trial enrolled 30 patients, of whom 14 received prednisone and acyclovir (200 mg 5 times a day for 10 days) and 16 received only prednisone. All achieved good recovery of facial motor function.[16] **Versus prednisone:** We found 1 RCT.[17] The trial was not blinded or placebo controlled, and the randomization technique was not stated. Of the 113 people enrolled, 12 (10.6%) were unavailable for follow-up, 54 received acyclovir, and 47 received prednisone. Prednisone therapy was associated with a significantly higher rate of good facial motor recovery (44/47 vs 42/54 with acyclovir, RR 0.83, 95% CI 0.71-0.98).

John Radcliffe Hospital/SPL

Acute paralysis occurs with equal frequency on the right and left sides of the face of patients with Bell's palsy

Harms

No serious adverse effects were reported in these trials.

Comment

The final trial comparing the use of acyclovir with that of prednisone was of poor quality and must be interpreted cautiously.[17]

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Vaccination updates

INTRODUCTION

New developments have occurred in vaccination, leading to changes in existing vaccines and vaccination policies in children and adults. The following information is based on reports that appeared in *Drug Therapy Topics* of the University of Washington Medical Center, Seattle.

UPDATES IN PEDIATRIC VACCINATION

Chickenpox vaccine

The Food and Drug Administration approved the nation's first chickenpox vaccine in 1995. The Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics now recommend immunizing children against the infection at 12 to 18 months of age. Approval followed rancorous debate about the need for universal vaccination against a self-limiting disease. Since its approval, many parents have expressed reluctance about giving their child yet another vaccine. A recent parental survey, however, suggested that parents feel positive about the vaccine's ability to prevent the rare but serious complications of chickenpox.[1]

The most persuasive evidence to date of the efficacy of chickenpox vaccination comes from a field study conducted by the CDC in an area north of Los Angeles. California has the highest chickenpox rates in the country. Five years after launching a voluntary chickenpox vaccination program, health officials found that inoculations can reduce cases by 80%.[2] The number of chickenpox cases in the region fell from 2,934 in 1995 to 587 by 1999. Rates declined in all age groups. The most impressive decline occurred in children ages 1 through 4 years. The vaccine also showed economic and social benefits. Infected children and their caretakers in the region missed 14,842 days of work and school in 1995 but only 2,718 days in 1999.

Based on these results, California will make chickenpox vaccination mandatory in 2001 for children entering its schools or day-care facilities. Half the states in the country now require the vaccination.

Combination vaccine use

A meeting at the National Institutes of Health concluded that combination vaccines, containing several antigenic components, are essential if physicians are to take full advantage of vaccines under development to treat childhood disease.

The number of injections now included or to be added to the pediatric immunization schedule is imposing an unacceptable burden on physicians and parents. The current schedule involves giving a child 19 to 23 injections by 6 years of age, 16 of them in the first 18 months. One way to minimize this burden is to combine the necessary agents into fewer vaccines. At issue is how to test such combinations for safety and efficacy.[3] Even the safety and efficacy of combination vaccines whose components are already licensed are not fully established.

Summary points

- Vaccination against chickenpox can reduce chickenpox rates, and it will become mandatory in California in 2001
- Combination vaccines can minimize the burden of having to give multiple injections to children
- Healthy children younger than 2 years are at high risk of influenza and may benefit from influenza vaccination
- Vaccinating health care workers against influenza reduces the risk of death among elderly patients
- It is now recommended that everyone older than 50 years receive the influenza vaccine

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Young children may benefit from influenza vaccination

Two independent studies have reported that healthy children younger than 2 years are hospitalized for influenza at higher rates than older children during the influenza season. The findings suggest that children in this age group are at high risk and should receive vaccination.

In 1 investigation, Neuzil and colleagues reviewed Medicaid files from 1973 to 1993 and identified healthy children up to age 15 years.[4] They examined hospitalization rates for acute cardiopulmonary conditions, outpatient visits, and the use of antibiotics during and out of influenza season. The average number of excess hospitalizations was 4 per 10,000 children per year for 5- to 15-year-olds. However, this number rose to 104 per 10,000 children per year for infants younger than 6 months. The excess number of outpatient visits was highest in those aged 6 to 12 months. Antibiotic use was far more prevalent in infants than in older children. The authors concluded, "The excess rate of hospitalization in [children younger than 1 year] is similar to rates in adults for whom an influenza virus vaccine is recommended."[4]

In a second investigation, Izurieta and associates studied children aged 18 years or younger in several cities who were enrolled in health maintenance organizations from 1992 to 1997. The research team examined hospitalization rates for acute respiratory disease during periods when the circulation of influenzaviruses predominated over that of respiratory syncytial virus. The hospitalization rate for low-risk children younger than 2 years was about 200 per

100,000 per month, similar to that for high-risk children aged 5 to 17 years. The hospitalization rate was more than 90% lower in low-risk 5- to 17-year-olds. The authors concluded, "Our study demonstrates increased rates of influenza-related hospitalization among children younger than 2 years of age and suggests that routine influenza vaccination should be considered in these children."[5]

An editorial accompanying these 2 papers cautions, "To justify routine influenza vaccination of infants and toddlers, the benefit-risk ratio would need to be very high."[6] The authors are concerned by "the relatively small proportion of cases of severe respiratory illness that would be prevented, the probable need for more than one dose, the uncertainties and unpredictability of antigenic variability, and the need to immunize during a period when many other vaccines are given."[6] They recommend that large controlled trials of infant and toddler influenza vaccination be done to evaluate safety, effectiveness, and cost-effectiveness.

UPDATES IN ADULT VACCINATION

Vaccinating health care workers reduces influenza-related deaths in elderly patients

Offering routine influenza vaccinations to health care workers in long-term care facilities has been shown to significantly reduce the risk of death among elderly patients.[7] In a randomized controlled trial that was carried out during a flu outbreak in the United Kingdom, the investigators offered or did not offer flu vaccine to the staff of 20 long-term care facilities. Only half of the health care workers who were offered flu vaccine were actually inoculated, compared with 5% of those who were not offered the vaccine. Nasal and throat swabs were taken for viral surveillance every 2 weeks from patients in these facilities during the outbreak. The researchers found that 13.6% of patients died in facilities where the staff was offered vaccine, which was significantly less than in the control facilities, where 22.4% died. The number of patients infected with influenza between the treatment and control facilities did not differ, however.

The findings suggest that a program of influenza vaccination of health care workers substantially lowers mortality among elderly patients, seemingly by reducing the severity of the infection. An accompanying editorial says that more studies are needed "before concrete steps are taken to routinely vaccinate health care workers."[8]

Vaccine modified for 2000-2001 influenza season

The influenza vaccine is changed every year to reflect the strains that infectious disease experts predict will circulate. The flu vaccine licensed in the United States is made from killed influenzaviruses, and it cannot cause infection.

This year, the CDC's Advisory Committee on Immunization Practices has decided to replace 2 of the 3 strains in the 1999-2000 vaccine and to lower the age for which a flu shot is recommended. The expert committee has now recommended that the vaccine be given to people aged 50 years and older because almost a third of the adults in this age group has 1 or more medical conditions that put them at high risk of flu-related hospitalization and death. Previously, the vaccine was recommended for people aged 65 and older.

Mark Clarke/SPL

Chickenpox vaccination is now recommended for all children 12 to 18 months of age

Most 1999-2000 cases of influenza infections were type A, and lapses in prevention were reported. According to the CDC, failure to immunize results in 20,000 to 40,000 flu-related deaths each year in the United States.

Manufacturing problems have delayed flu vaccine

Officials at the CDC disclosed that the shipments of influenza vaccine for the 2000 flu season will be delayed and that there may be shortages because of manufacturing problems. The agency told clinics, hospitals, and other providers of health care to delay mass immunization campaigns for at least a month and to prepare to immunize people at highest risk first. The chief of the influenza branch of the CDC described the delay as follows: "We have never had a situation where all manufacturers were having a similar problem with a strain."[9]

The announcement of the delay came at a time when health officials expected that a record number of Americans, perhaps as many as 75 million, would be immunized because of the lowering of the age to 50 years when all persons are advised to get immunization.

Drug Therapy Topics is a monthly publication from the University of Washington–Harborview Medical Center Drug Information Center. The full text is freely available at http://depts.washington.edu/druginfo.

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Netphiles

We welcome suggestions for Web sites to be included in future Netphiles

Older parents

Older parents are not only less likely to conceive, but also more likely to have a bad outcome from their pregnancy (*BMJ* 2000;320:1708-1712).

The human cost of all this is clearly expressed on the Internet. Hannah's Prayer (www.hannah.org/), which has a nondenominational Christian character, links a wide range of resources for women who have lost pregnancies or had stillborn infants. There are also "down the line" health care resources. Searching for information on this well-recognized topic is harder than I thought it would be. The conventional medical portals such as OMNI (www.omni.ac.uk) have lots of general information about pregnancy but little specific on this issue.

The most promising new resource I have encountered is the Open Directory Project (www.dmoz.org/), which, like Yahoo, is a human-edited directory. Unlike Yahoo, it has 25,930 volunteer editors (at the last count) indexing 279,491 categories. Their efforts are made freely available by using an open license and, plainly, their combined might has the potential to overwhelm any commercial venture. It at least produced some relevant hits, a personal account of pregnancy in later years (www.thelaboroflove.com/forum/jan/1.html), and links to consumer resources such as BabyZone (babyzone.com/family.htm).

But the legendary personalization that the Internet is supposed to enable was not much in evidence on BabyZone: zapping advertisements for baby products alongside content aimed at subfertile women and the mothers of recently stillborn infants seems tactless. One way to avoid such offenses would be to accept remaining childless: www.moretolife.co.uk/ offers a support organization for would-be parents who cannot have children.

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Curbside Consult

Exercise for cancer patients: a new challenge in sports medicine

In the past, physicians usually advised patients with chronic diseases to rest and avoid physical effort. These recommendations were empirical: because most chronic diseases are associated with functional changes resulting in impaired physical performance, exercise in this group of patients may generate fatigue, breathlessness, and tachycardia. Therefore, avoiding physical activity results in less discomfort.

Exercise could play a role as complementary therapy for cancer patients during and after treatment

In the past few years, however, scientific evidence has dramatically changed our ideas about exercise for patients with chronic diseases. In the late 1960s, the inclusion of physical activity in rehabilitation programs for patients who had had myocardial infarction set a milestone and opened up new perspectives for the use of exercise in the treatment of chronic diseases. It is now well established that excessive rest and lack of physical activity may result in severe deconditioning and, thus, reduce the functional status and quality of life of patients with chronic illness. Furthermore, numerous studies have shown that exercise is an effective means for counteracting several of the adverse effects that chronic diseases have on physical performance. As a result of this evidence, exercise is actually considered an essential component in the treatment of several illnesses, including peripheral vascular disorders, chronic obstructive lung disease, ischemic myocardial disease, and heart failure. The value of exercise for rehabilitation has been widely recognized; indeed, many institutions offer exercise programs for organ transplant recipients and for patients after myocardial infarction or with chronic renal failure. Until recently, however, less was known about the feasibility and effects of exercise programs for cancer patients during and after treatment.

The role of exercise in oncologic rehabilitation programs has thus far been mostly limited to physical treatment addressing specific impairments caused, for example, by amputation or surgery. However, the medical attitude regarding exercise for cancer patients is changing fast. The recent world class performances of athletes who have been treated for cancer have focused attention on the effects of training on the physical performance of cancer patients. Moreover, recent studies have shown that physical activity may improve the quality of life, mood, and the physical performance of cancer patients during and after treatment.

Regular physical activity has been shown to increase the performance status in breast cancer patients treated with conventional chemotherapy[1] and in patients after bone marrow transplantation.[2] It has also been shown to reduce psychological distress and fatigue in patients treated with radiotherapy[3] and after high-dose chemotherapy with peripheral blood stem cell transplantation.[4] Furthermore, a reduction of treatment-related complications has been observed in cancer patients participating in exercise programs during cancer treatment.[5,6] Finally, preliminary evidence suggests that regular physical activity may improve immune function.[7-9] Therefore, exercise could play a role as complementary therapy for cancer patients during and after treatment.

More information is needed, however, about the effects and feasibility of exercise programs for different groups of patients with oncologic diseases. Indeed, "cancer" is a common denominator for more than 100 neoplastic diseases, each with a different cause, course, and prognosis. The natural history of the same nosologic disorder may vary considerably in different settings—that is, acute lymphoblastic leukemia in children and adults. Finally, cancer patients may have many specific problems. Chemotherapy can damage bone marrow and thereby impair the production of red blood cells; the resulting anemia decreases the oxygen transport capacity of the blood. Agents like anthracyclines and cyclophosphamide and irradiation of the mediastinum can result in myocardial damage and a decrease of cardiac output. Metastatic disease and pleural effusion cause a reduction of total lung capacity; furthermore, changes in the pulmonary architecture due to surgical treatment of primary or metastatic lung cancer or as sequelae to fibrosis after radiotherapy may alter the ventilation-to-perfusion ratio. Treatment with immunosuppressive agents (for example, high-dose corticosteroids and cyclosporine) can lead to a marked loss of muscle mass and severe myopathy. Furthermore, reduced protein and calorie intake as a consequence of anorexia and nausea and impaired absorption after gastrointestinal surgery may lead to a negative nitrogen balance and, hence, to a catabolic state. Finally, an increase in the concentration of cytokines—interleukins 1 and 6, tumor necrosis factor, and alpha interferon—resulting from the interaction between the tumor and the host-defense system has been

associated with muscular waning. All these factors may affect patients' physical condition and reduce their performance and must be carefully considered when designing an exercise program.

Research about the effects of exercise in the prevention and rehabilitation of cancer and of physical activity on immune function is still at its beginning. However, this is going to be one of the most active areas of research in sports medicine in the coming decade. It is certainly time to meet the challenge.

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Are phytoestrogens a "natural alternative" to estrogen replacement therapy?

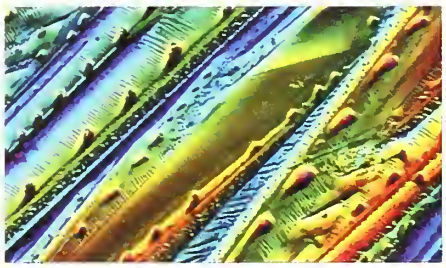
Phytoestrogens, compounds derived from plants and converted into weak estrogenic substances in the gastrointestinal tract, are heavily promoted as the "natural alternative" to estrogen replacement therapy for postmenopausal women or women who have undergone a hysterectomy. The use of soy products rich in these phytoestrogens is now widespread in the United States.

Isoflavones are the best-known phytoestrogens, but only a few studies have been done of their effects. The results of these studies have not been promising. Their supposed benefits are based on the observation that the incidence of certain disorders or diseases affected by estrogen status—perimenopausal syndrome, cardiovascular disease, and osteoporosis—is lower in populations with diets high in phytoestrogens. There is no laboratory or clinical evidence to support claims of benefit or even to demonstrate hormonal effects of phytoestrogens. A recent commentary on phytoestrogens concluded: "Until such time as there are data from controlled studies on the dangers as well as the benefits of plant extracts, the drawing of firm conclusions about the long-term benefits of increased phyto-oestrogen consumption is unwise."[1(p164)]

For most of the world's population, the principal source of phytoestrogen is soy in the diet. Since October 1999, the Food and Drug Administration has allowed food companies to claim that soy protein reduces cholesterol concentrations and the risk of heart disease. Although consuming soy products seems to reduce cholesterol levels, there may be an increased cancer risk associated with their isoflavone components; this risk may be heightened when isoflavones alone are offered in the form of dietary supplements.

The highest levels of naturally occurring isoflavones are found in soy beverages, cooked soybeans, and tempeh (textured fermented soy). One gram of soybeans contains about 1 mg of isoflavones. Some nutritional experts are willing to assume that a daily intake of 50 mg of isoflavones is safe. The typical daily consumption in Japan is 25 to 50 mg of isoflavones. Dietary supplements, however, can contain more than 85 mg of isoflavones in a single unit, and some manufacturers advise taking 2 a day.

Soy protein concentrate powders have as much as 160 mg of isoflavones per serving.



Michael W Davidson/Florida State University

Soy is the principal dietary source of phytoestrogens

According to some evidence, large quantities of isoflavones may increase the risk of breast cancer.

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When should physicians forgo curative treatment of pneumonia in patients with dementia?

Using a guideline for decision-making

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Summary points

- We have developed a guideline to help physicians to decide whether to forgo curative treatment of pneumonia in patients with dementia who live in nursing homes
- Decisions should take into account the medical aspects of each patient, the patient's autonomy and preferences, and if preferences are unclear, the patient's best interest
- The decision-making process may involve the family, nurses, and physicians, but the treating physician should ultimately decide
- Our guideline is useful mostly for complex cases, such as when patients' wishes are unclear or when their family and health professionals have opposing views

THE ETHICAL DILEMMA

The prognosis for a nursing-home patient with pneumonia is uncertain.[1] It is, therefore, hard to predict whether antibiotics and hydration—given to such patients with curative intent—turn out to be futile treatments. If patients die within a few days, they may well have suffered from the burden of receiving intravenous drugs and fluids. On the other hand, such treatments may actually reduce symptoms and, thus, suffering.

With demented patients, such treatment decisions are further complicated by ethical and legal issues. The patients' wishes are often unclear because they cannot competently evaluate the situation or communicate their wishes. The decision-making process is, therefore, complex and multifactorial.[2-4]

The *Western Journal of Medicine* recently published guidelines on "nonbeneficial or futile medical treatment," divided into those for patients with and those without decision-making capacity.[5] These were referred to as "conflict resolution guidelines." Although we acknowledge that roles and responsibilities in such guidelines need to be clear, additional dimensions need to be addressed.

With international support, as a Dutch research group, we developed a guideline aimed at supporting prudent decision-making for demented patients. This may prevent conflicts because it contributes to better decision-making. In this article, we briefly review the development and evaluation of our guideline. We then discuss how this guideline can be applied to clinical practice, an issue of interest to both clinicians and policymakers.

DEVELOPING OUR GUIDELINE

The guideline was developed for use by nursing-home physicians. It clarifies the steps that should be taken in the decision-making process when deciding whether to forgo curative treatment of pneumonia in demented nursing-home patients. When curative treatment is forgone, palliative treatment should be started.

Full details of how we developed our guideline have been published elsewhere.[6] Briefly, a "checklist of considerations" was drawn up, based on a literature review, discussion papers of Dutch medical associations, and consensus procedures with experienced nursing-home physicians and international experts in the fields of nursing-home medicine, ethics, and law.[7-10] This checklist was then piloted in clinical practice. Finally, a revised checklist was endorsed by all experts and authorized by the Dutch professional organization of nursing home physicians (NVVA) for use in a prospective study.

The checklist of considerations

The checklist of considerations, shown in part in figures 1 and 2, divides the decision-making process into 3 main areas: medical aspects, patients' autonomy and preferences, and patients' best interests.

Medical aspects

Little evidence exists to guide the medical aspects of the decision to treat curatively or palliatively. This aspect of the checklist addresses the expected outcome with curative treatment versus forgoing curative treatment (administering palliative care) and the burden of any curative treatment.

Autonomy and the best interests of the patient

The emphasis of the other 2 areas is on ethical and legal aspects. The checklist is based on well-known ethical principles that should guide physicians, including respect for autonomy, the duty to do good, doing no harm, and justice.[8]

In Dutch culture and law, patient autonomy is highly valued.[11] If patients are competent to make a decision, physicians must respect their wishes. If they lack the capacity to make a decision but have made a living will, then their wishes in the will should be respected. If no living will is available, patients' representatives—a curator or mentor, family, or friends—are asked. The professional carers should incorporate this information to try to determine patients' wishes.

If patients' wishes remain unclear, the last area of the checklist, discussing "the patient's best interest" can guide decisions. Both the representatives and the professional carers, including the responsible physician, are allowed to state what they think would be in the patient's best interests. Finally, the responsible physician decides on the treatment.

Case 1

Mrs K, a widow with 1 daughter, was admitted to our nursing home with advanced vascular dementia. She had lived in a residential home but now required nursing care. She was disoriented, with severe cognitive impairment, aphasia, apraxia, and withdrawn behavior. She used a wheelchair and needed extensive help with her personal hygiene. During her stay, she developed depression. Despite medication, she was often restless, sad, or agitated. Her food and fluid intake was marginal despite dietician and nursing intervention. Advanced care planning had not taken place on admission.

Six months after admission, she developed pneumonia and was at risk of dehydration. Based on the "checklist of considerations," we considered that a curative treatment would be effective only in part. We might have achieved cure but at the expense of an even lower level of physical and mental functioning because her health had been deteriorating during the past month. If cured, we expected her to suffer from a recurrent infection in the near future. Curative treatment seemed burdensome, given her restlessness—we would have to bind an intravenous line to her arm.

We contacted Mrs K's daughter, explaining the situation and the possible consequences of curative and noncurative treatment. Mrs K's wishes were not clear. She had not been capable of communicating this during her stay, she had no written will, and there was no other indication of what she would have wanted.

Considering what was in "the patient's best interest" (from the checklist), the daughter acknowledged that her mother's health was poor and that cure was unlikely. However, she judged that curative treatment should be given because she would not make a decision leading to her mother's death.

The last section of the checklist guided us through this difficult situation in which the physicians, nursing staff, and some of the family agreed on the treatment that was in the patient's best interests, but the daughter was unhappy about withholding a potentially curative treatment. Although the treating physician was responsible for deciding on Mrs K's treatment, we ideally wished to make a consensus decision. We therefore talked with Mrs K's daughter again. We explained that Mrs K's prognosis was poor, even with antibiotics. Her daughter agreed that she could not let her own feelings rule over what was in her mother's best interests. Mrs K received palliative treatment and died 4 days later.

The checklist was useful in this complex case, allowing us to consider the important issues in a systematic way. Although it did not help us in estimating her quality of life, or lack of pleasure in life, it did help us to look at the situation more objectively. It forced us to keep thinking and talking about the best decision.

EMGO/HVSG *Vrije* Universiteit *Amsterdam*

Points to consider in the decision process for starting or not starting a curative treatment of a pneumonia in psychogeriatric patients

Instruction
The list has been constructed as a questionnaire. Every section ends with a concluding question, after which is included a block with explanatory text, which refers to a part of, or all answer categories. Hereafter one is led to the next section which is applicable to this patient. The last page but one consists of a summarizing survey (section D.), which one should fill out to visualize the main con-siderations on one page to be of use for the decision process.

The purpose of this list of 'points to consider' is to *assist* nursing home physicians in the decision-process for starting or not starting a curative treatment of a pneumonia in psychogeriatric nursing home patients. The list is ***not designed to direct the physician*** to a certain treatment decision. Structuring the decision process is done by *carefully and systematically recording* some medical aspects, and especially the aspects that are important to consider in the decision process from a legal and ethical point of view. Naturally, in all cases the responsibility for the final decision lies in the hands of the responsible treating physician.
The main guiding variables in the decision process are
1 the expected *effect* of a curative treatment from the medical perspective.
2 the patient's *wish* a living will, or the reconstruction of the wish,
3 the patient's *best interest* in case the wish of the patient is not clear, or remains unknown.

Definitions

(Intentionally) curative treatment of pneumonia a treatment of a pneumonia that has achieving cure as the primary goal. Explanation: this is irrespective of the chance of success of curing pneumonia. The treatment consists of antibiotics, which can be combined with (re)hydration. Nevertheless, the course of the disease may necessitate installing palliative treatment as well.

Palliative treatment of pneumonia, a treatment whose primary goal is not cure, but is aimed at treating the symptoms of the pneumonia. Explanation: the aim of this is to improve the patient's wellbeing and quality of life. Palliative use of antibiotics -when achieving cure is not the primary goal- can be meant by this as well.

Experts

The following experts have commented on the list with points to consider, and have subsequently subscribed to the list.

J.J.M. van Delden, MD, PhD (The Netherlands)
Prof. H.M. Dupuis, PhD (The Netherlands)
L. Emanuel, MD, PhD (U.S.A.)
C.M.P.M. Hertogh, MD, PhD (The Netherlands)
A. Hoogerwerf, MD (The Netherlands)
Prof. H. Kuhse, PhD, (Australia)
Prof. H.D.C. Roscam Abbing, LLD (The Netherlands)
Prof. J.M. Stanley (U.S.A.)

This list with points to consider has been autorized by the Dutch Society for Nursing Home Physicians (NVVA) for the present, in behalf of a study after pneumonia.

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Figure 1 Slightly adapted version of the front page of the "checklist of considerations" (from the Institute for Research in Extramural Medicine [*Instituut voor Extramuraal Geneeskundig Onderzoek*; EMGO]/Department of General Practice, Nursing Home Medicine and Social Medicine [*Vakgroep Huisarts, Verpleeghuis–en Sociale Geneeskund*; HVSG] Vrije Universiteit Amsterdam)

USING THE CHECKLIST IN CLINICAL PRACTICE

The checklist was introduced during an observational study on the clinical course of pneumonia in Dutch nurs-

D. Summarizing survey of the checklist of considerations

Copy the results of the preceding pages, as far as applicable.
Filling out part D is optional, however, part E should be filled out

A.1.6 Is an intentionally curative treatment indicated for this patient?

☐ Yes, indicated	I don't know	☐ No, not indicated

A physician is not compelled to act if this is not medically effective. Moreover, a request to treat cannot be honored if the treatment at issue is not in agreement with the medical professional standards. According to -among others- CAL, starting a treatment is undesirable if it is considered to be not medically effective, irrespective the wishes and opinions of the patient and other persons involved.
There should be a dialogue, however, with the nursing staff and the patient's representative(s), explaining the undesirability of installing treatment that is not effective.

A.2.3 How physically and/or psychically burdensome would the total curative treatment -antibiotics and (re)hydration- be for the patient?

Very burdensome	☐ Somewhat burdensome	☐ Not or little burdensome

When choosing the best treatment, beside the medical effectivity, the burden of treatment plays a part.

B.1.4 Is the patient sufficiently mentally competent, and if so, what treatment does the patient want?

☐ Insufficiently competent	☐ Sufficiently competent, wants curative treatment	☐ Sufficiently competent, wants palliative treatment

In this situation, merely the present wish of the patient applies and the rules for informed consent must be adhered to. Neither a written will, nor family or representative(s) do play a role in the decision process.

B.2.9 What is the purport of the written will?

☐ Unclear/absent	☐ Patient wants curative treatment	☐ Patient wants palliative treatment

In the WGBO a 'negative written will' has been given a legal status. A physician is compelled to follow the will when the patient does not wish a curative treatment, unless there are sufficient grounds (as mentioned in B.2.5 - B.2.8) not to do so.
As a rule, there should be a dialogue with the nursing staff and the patient's representative(s). The written will, however, is decisive.

B.3.9 What is the purport of the reconstruction of the patient's will according to the representative(s)?

☐ Absent / doubt / opposing opinions	☐ Intentionally curative treatment	☐ Palliative treatment

According to the WGBO, appointed as well as unappointed representatives have the authority to take decisions on the patient's behalf. The physician, however, retains his or her responsibility to test these decisions for medical effectiveness, and whether the representatives are actually reconstructing the wish of the patient (which has been tested in part B.3).

B 4.7 What is the purport of the reconstructed patient's wish according to the other involved professional carers?

☐ Doubt / opposing opinions	☐ Intentionally curative treatment	☐ Palliative treatment

The nursing staff and other (para)medics are not authorized to make decisions. The treating physician retains this responsibility.

C.5 Which treatment seems to be in the patient's best interest?

☐ Doubt / opposing opinions	☐ Intentionally curative treatment	☐ Palliative treatment

Finally, the physician bases his or her choice of the treatment on what is in the patient's best interest.

Figure 2 Part D of the decision-making questionnaire. WGBO = Dutch law on the medical treatment agreement (*Wet op de Geneeskundige Behandelings Overeenkomst*).

ing homes. For more than a year, use of the checklist was promoted but was not mandatory. The completed checklists were returned to the researchers.

The use of the checklist in these nursing homes has been evaluated (J T S, M E O, M W R, G W: "Decisions to Treat or Not to Treat Pneumonia in Demented Psychogeriatric Nursing Home Patients: Evaluation of a Guideline," unpublished data, date?). It was used in 50 of the 61 participating nursing homes and for about half of the patients (n = 228). Contrary to our expectations, the checklist was used as often in decisions about curative as about palliative treatment. It was used more often for less complex cases, such as when advanced care planning had already taken place. Nursing-home physicians did not use the checklist if the decision was already clear. Most physicians used it to confirm that they had the right decision in mind.

CASE HISTORIES

The 2 case histories were provided by 1 of us (T de G), who is a nursing-home physician and local coordinator of the Pneumonia Study in the Oostergouw Nursing Home. The cases are based on composites of 15 cases so as to protect the confidentiality of individual patients.

Case 2

Mrs B, a widow with 1 son, was admitted to the nursing home when she was 80 years old. She had lived alone, and it was becoming unsafe for her to cook meals. She had early Alzheimer's dementia and was disoriented, with diffuse memory disturbance and mild apraxia. She socialized well on the ward and seemed content. She was able to walk independently and needed minimal help with washing and dressing.

Her son visited her frequently. We discussed with him what should happen if his mother were to become unwell with an intercurrent illness. We decided that life-sustaining measures would be appropriate if they carried a high likelihood of cure.

When Mrs B developed symptoms and signs of bacterial pneumonia, we used the checklist of considerations in guiding us toward a decision. The first section—on medical aspects—was easy to fill out. Because her preexisting health was relatively good, we expected her to recover quickly from the pneumonia without any adverse effects of the treatment. Therefore, estimating her life expectancy, which was requested in this section, seemed pointless. We could not think of any burden of curative treatment because she was able to take oral antibiotics.

The next sections of the checklist concerned Mrs B's wishes. Her competence to understand her situation was moderately to severely impaired. We, therefore, did not want to discuss the progressive nature of the dementia with her or her limited life expectancy. Although she knew she was currently ill, Mrs B had no insight into the long-term consequences of any treatment and would not have given a reliable opinion. We told her that she had an "inflammation" of her lungs and that we would treat it. We contacted the family and nursing staff, who agreed that curative treatment was appropriate.

Mrs B was well within 4 days of antibiotic therapy and returned to her level of functioning before the pneumonia. In this case, because curative treatment carried little burden, the prognosis was good, and the patient's wishes had been discussed previously, the checklist provided little additional help in decision-making.

CONCLUSIONS

Development of the checklist involved translating *principles,* which were general guides, into *rules,* which were more specific to the decision to forgo antibiotic treatment in demented patients.[8] The next step will be to translate these rules to specific situations and apply the checklist in treatment decisions about individual patients. Because of the diversity of clinical contexts, this step may be even more challenging than the first. Forgoing curative treatment in demented patients suffering from pneumonia is a difficult and delicate decision.

An important ethical issue, as yet unresolved, is the application of the principle of autonomy to demented patients. The "protected milieu of autonomy" should be as inclusive as possible in demented patients.[12] Living wills are rarely available in these patients, at least in the Netherlands, making it more difficult to interpret patients' wishes. Patients with dementia may no longer be aware of their situation and the future, but they may enjoy other aspects of life. Insights from "ethics of care" may provide additional ways of dealing with this issue of former and current wishes.[13,14]

We hope that our checklist is used for supporting and guiding decisions, rather than being used in a purely directive way or only to confirm previous decisions. Physicians' responsibility does not end with the checklist. Instead, it is extended by the decision whether to use the checklist to optimize decision-making.

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COMMENTARY

Pneumonia, friend of the elderly

Must we rescue everyone we can? Should our ability to do something work against us, at times obliging us to act against our better judgment? We can cure even elderly, demented people of pneumonia, but not everyone will consider this a morally compelling argument for doing so.

In the decades since we learned to treat pneumonia, the life expectancy in western nations has increased significantly. More and more elderly people will come down with pneumonia in the years to come. How should we think of pneumonia, in the elderly or anyone else? There is good reason to think of pneumonia as a blessing in some cases, specifically in elderly, demented persons.

This is not the place to argue for the morality of this perspective. The article by van der Steen and colleagues begins from the reasonable premise that pneumonia may signal a welcome way out of suffering. Their article will do nothing to change the mind of anyone who insists we must always work to cure elderly persons of pneumonia. It will, however, offer useful guidance to families of elderly, demented nursing-home patients and the physicians who treat such patients.

The very idea of a checklist rests on the notion that decisions should be made on the basis of persons, who will naturally differ in circumstances, as opposed to principles, which by definition do not vary. The checklist seeks to guide caretakers of incompetent patients to make arduous decisions about both curative and palliative care. The checklist responds to the absence of an advance directive or "living will." Relatively few Americans have prepared such documents: many do not know about them whereas others avoid thinking about them. Even if we do prepare advance directives, physicians do not always honor them. Presumably any physician who would agree to withhold treatment from an elderly, demented patient would also

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agree to honor an advance directive requesting this be done. The advance directive would make this decision easier for all concerned.

The most important benefit of this checklist from the Netherlands is to help break up a complex question into more manageable segments. Faced with a difficult decision, many of us will respond in the same way as the daughter in case 1—we may feel morally compelled to do everything possible for a demented parent in a nursing home. On further reflection, specifically on the questions brought out by the checklist, we may feel more reluctant than compelled. This is progress.

Beyond guiding our deliberation in an enormously trying moment, the checklist serves a broader purpose. It gives us permission to think in concrete terms about the quality of someone else's life. The checklist facilitates the enormously difficult task of deciding for others. It allows us to consider whether pneumonia may be a blessing instead of a burden.

This checklist returns us to a familiar debate over the morality of withholding and withdrawing medical treatment. Most primary care physicians and bioethicists in the United States will likely embrace this checklist as a useful and welcome resource.

Filipino attitudes toward pain medication

A lesson in cross-cultural care

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Information about cultural patterns presented in this article and others in this series represents generalizations, which should not be mistaken for stereotypes. Cultural generalizations will not fit every patient, but awareness of broad patterns can give practitioners a starting point from which to provide appropriate care. The information on Filipino symptom management in this essay is taken from R Cantos and E Rivera's chapter in *Culture and Nursing Care: A Pocket Guide,* edited by J G Lipson, S L Dibble, and P A Minarek and published by University of California, San Francisco, Nursing Press (1996).

One of the comments I frequently hear in my nursing classes is that there is a tendency among Filipino nurses to undermedicate their patients who are having pain. I am told that if a physician prescribes a range of dosages, they will often choose to administer the lowest dose. One evening, I decided to ask the Filipino students in my class if that were really the case and, if so, why. Many of them agreed with the statement and offered me a number of explanations, including that pain medication is scarce in the Philippines, so they are trained to use as little as possible to make it go further. Among other reasons is that stoicism is highly valued and, for Catholic Filipinos, suffering is an opportunity to demonstrate virtue.

A few minutes into the discussion, I noticed tears falling from the eyes of one of the Filipino students. When I asked Cecilia what was wrong, she quietly explained that her mother had died of cancer a year earlier. Because she was a nurse, the hospice had arranged for her to administer the strong dosages of medication necessary to ease her mother's pain. Cecilia did so, but automatically cut the dosages in half before giving the medication. She certainly did not want her mother to become a drug addict. Besides, her mother never complained about not getting enough medication.

Now, through the class discussions, she realized that her long-ingrained habits and attitudes toward pain medication had caused her mother needless suffering. Her mother was dying; "addiction" was a meaningless concept at this point in her life. But her mother was gone, and there was nothing she could do to make up for it.[1]

PAIN (*MASAKIT*)

Most Filipinos can be stoic, so do not rely on the expression of pain to determine a person's level of pain. Offer pain medications as ordered. Some patients have a high pain threshold. Understand the numeric scale of expressing pain. Filipinos are fearful of becoming addicted to narcotics. They hate shots, preferring to take medications by mouth or through an intravenous drip. Offer warm

Aaron Favila/AP

Filipinos characteristically are stoic in the face of pain

compress when necessary. Some will moan as a way of expressing pain.

DYSPNEA (*HINDI MAKAHINGA* ["CAN'T BREATHE"])

Filipinos tend to get frantic when dyspneic. They will hyperventilate and will use oxygen after some explanation. Some will be more anxious about using oxygen, associating its use with greater gravity of disease.

NAUSEA AND VOMITING (*NASUSUKA* ["NAUSEATED"])

Because of modesty and shame, a Filipino patient will alert a nurse after vomiting. Some will clean up or throw away vomitus. Some will ask the nurse for nausea medication.

CONSTIPATION OR DIARRHEA

Filipinos become uncomfortable if routine bowel movement is disrupted. Because of modesty, they will disclose this to a nurse only when asked. They will accept measures to correct alteration in bowel functions, but enemas are used only as a last resort.

FATIGUE (*PAGOD* ["TIRED"])

Filipinos are accustomed to taking naps in early afternoon. They hesitate to use sleeping pills for fear of addiction.

DEPRESSION (*LUNGKOT* ["SAD"])

Because of shame, they will not acknowledge depression to health care professionals unless asked.

SELF-CARE FOR SYMPTOM MANAGEMENT

Filipinos do not respond to illness until it is advanced, they have taken to bed, or are in severe pain.

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Physician-patient relationship: like marriage, without the romance

Physicians and philosophers have contributed to the field of medical ethics several different paradigms for the physician-patient relationship. I suggest another: marriage. Patients usually enter relationships as we enter marriage: we allow our high hopes to obscure the possibility of deep disappointment. The argument of the essay is to refocus on the contractual element of the physician-patient relationship.

Try as we might to overcome our emotions, they sometimes withstand even our best efforts. Particularly in medical care, fear and hope abound. Physicians and patients both would do well to consider how emotions can infiltrate our efforts to think clearly.

What kind of physician could keep her emotions under lock and key? Only one most of us would prefer to avoid. A reading of Aristotle, who links pity to fear, suggests that compassionate physicians may pity their patients for 2 reasons, 1 other-regarding (sadness about a patient) and the other self-regarding (fear that the physician could end up in the same condition). In *Rhetoric* (book 2, chapter 5), Aristotle states that, generally speaking, the same misfortunes that cause us to pity others elicit real fear when they happen to us.[1(p1390)] He does not exactly say that fear and pity differ only in whether the misfortune happens to us or to someone else; his point is, rather, to balance these psychological reactions on a fulcrum of emotional closeness. These emotions arise in the context of caring for others: Aristotle believes that we can only fear for other people or pity them if they matter to us in some important sense (*Rhetoric:* book 2, chapter 8).[1(pp1397-1398)]

Sick people want help. They naturally invest hope in the physicians they find. I want to examine the idea that patients as a group dislike thinking unpleasant thoughts. (No doubt physicians do, too, although probably less so in the health care setting.) A study demonstrated that most patients who have not discussed preferences for end-of-life care do not want to do so.[2] Most patients and physicians have not discussed end-of-life decisions, and most patients have not completed advance directives. A culture heavily invested in "the power of positive thinking" produces patients who may resist thinking about the possibility that their physicians will disappoint them. Do caring physicians reinforce their patients' natural aversion to bad thoughts?

So general a question cannot be answered definitively. However, something approximating an answer emerges from comparing the patient-physician relationship with marriage. Various scholars have pointed out the peculiarity of our relatively recent and predominantly western notion that marriage should be based on love.[3-5] Even after the Roman Catholic Church came to characterize marriage as

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a sacrament—that is, a means through which to encounter God—many families regarded marriage as a largely economic arrangement. A dowry could determine a woman's fate. The romantic or erotic aspect aside, marriage more closely resembles patient-physician relationships than friendship, for friendship does not involve a legal agreement. The stakes in both marriage and patient-physician relationships loom higher than in friendship.

Patients and physicians alike hope for a happy ending—and appropriately so. For this reason, patients and physicians have something important to learn from prospective spouses.

WHEN PATIENTS AND PHYSICIANS MEET

Virtually all patients hope, and some even hope against hope. Few surrender immediately to their illnesses. Biotechnology has given patients more reason to hope, even to hope against hope. Broad-based astonishment at the extraordinary progress of medicine in the past few decades is a cultural phenomenon of which physicians must be aware if they are to understand the expectations of patients.

Physicians naturally hope for the best for their patients as well. That physicians should establish better "connections" with their patients has become a regular theme in the literature of biomedical ethics.[6] Some writers in this field do a better job than others of bringing out the possible risks of establishing closer relationships with patients. One physician claimed in *The Journal of the American Medical Association*: "for me, fulfillment comes from the sudden intimacies with total strangers—those moments when the human barrier cracks open to reveal what is most secret and inarticulate."[7] Another physician has strongly urged empathy in clinical encounters and has argued that passion is a part of that empathy.[8]

Some patients expect their physicians to fill the role of a powerful paternal or maternal figure.[9] By the same token, some physicians are comfortable only in relationships in which they are taking care of and controlling others.[10] Even aside from relatively marginal cases, emotions can pervade physician-patient relationships.

No matter what else it aims to be, the patient-physician relationship is a contract involving the exchange of money and services. Timothy Quill has specified that 4 assumptions underlie the physician-patient contract: both the physician and the patient have unique responsibilities; the physician-patient relationship is consensual, not obligatory; both the physician and the patient must be willing to negotiate; and physician and patient each must gain something in their encounters.[11] Nothing in this list contradicts a contractual description of marriage, which similarly stands on an exchange of money and services.

Many experts in the field of biomedical ethics agree that the patient-physician relationship is more a covenant than a contract. This is not to say, however, that consensus exists on this point. The western institution of marriage represents both a covenant and a contract. Broadly speaking, western culture leads people to view matrimony as a covenant and, in so doing, encourages them to ignore the contractual nature of the institution. Married persons who face divorce for the first time frequently come to view the institution very differently—that is, as a contract. Patients disappointed by their medical care may well take a similar mental turn. Many medical malpractice suits begin in this way.

WHEN PROSPECTIVE SPOUSES MEET

Aristotle marries fear and pity in a way that requires emotional proximity. Although he does not mean or even mention marriage, he introduces the notion of affective ties in a way that makes marriage relevant to a discussion of what happens when physicians and patients meet. Just as prospective spouses focus on positive outcomes, so, too, do prospective physicians and patients work from a natural aversion to bad thoughts. What can physicians and patients learn from the legal institution of marriage?

The American legal scholar Lynn Baker has usefully illuminated the contractual nature of marriage. She points out that although little about the present legal procedures for getting married would cause one to think that a contract is being entered into, the law has long explicitly characterized marriage as a legal "contract" among husband, wife, and the state.[12] When people marry, they agree to be bound by the various laws that constitute the

implied terms of the marriage contract. At the time people apply for a marriage license, the state necessarily possesses the most complete possible knowledge of the legal terms of the marriage contract; however, it generally does not take any action to disclose even a portion of that information to the parties requesting to be married. Nor does the state require spouses-to-be to demonstrate that they have grasped the terms of the contract into which they are about to enter. I take Baker's point to apply to European marriages as well as to American ones, although I acknowledge differences between the 2 (for example, monetary settlements for both divorce and malpractice tend to be higher in the United States).

Baker's writings raise a question regarding informed consent for people engaged to be married that extends naturally to people in search of a physician: why is it that the law does not compel patients to learn before choosing a physician what the legal character and consequences of their acts are and, further, help them to predict with reasonable certainty the outcome of any subsequent adjudication regarding possible adverse outcomes? Baker has elsewhere argued that people simply do not wish to consider the possible adverse outcomes of a marriage contract. She has written,[13]

> [W]e . . . seem to believe that knowledge of the law, even taken alone, is not always and unambiguously better than ignorance. For sometimes that knowledge comes at the cost of dimming, if not entirely dispelling, our most precious ideals and cherished hopes. And that price is one we cannot afford to pay.

Prompting patients and potential patients to view their relationships with physicians as a covenant may be grounded in, and appeal to, their hope for recovery and may result in a susceptibility to overlook the contractual nature of their interaction with a physician.

In a separate work, Baker surveyed marriage license applicants and law students about their knowledge of divorce statutes and of the demographics of divorce and their expectations for their own marriage.[14] Both groups had largely incorrect perceptions of the legal terms of the marriage contract as embodied in divorce statutes, but both groups had relatively accurate, if sometimes optimistic, perceptions of both the likelihood and the effects of divorce in the population at large. These same persons expressed thoroughly idealistic expectations about both the longevity of their own marriages and the consequences of divorce. Increasing people's knowledge of divorce statutes through a course on family law did not diminish this unrealistic optimism. Baker's findings strongly suggest that the sense of surprise that frequently attends divorce may be a result of systematic cognitive biases rather than a lack of information about divorce.

Respondents' predictions for the permanence of their own marriages and the consequences should they be divorced were much more optimistic than their perceptions of the likelihood and effects of divorce on others. For example, although their median estimate that 50% of American couples who marry will divorce was accurate, the median response of the marriage license applicants when assessing the likelihood that they personally would divorce was 0%.

AVERSION TO BAD THOUGHTS

After reading Baker's work, we more readily understand why prenuptial contracts are so rarely used and their lack so often regretted. Baker's work may have something to say to clinicians who ponder why so few people have drawn up advance directives about end-of-life health care. The kind of thinking about patient-physician relationships outlined by the articles cited here discourages questions about malpractice or unhappy endings. Just as persons tend strongly to dislike considering possible adverse outcomes of matrimony, they may strongly dislike thoughts of adverse outcomes with physicians.

Perhaps the easiest way to avoid thinking of an unappealing possibility is to ignore the contractual nature of the relationship and to view that relationship as a loving covenant instead. For physicians, the importance of negotiating a proclivity to pity or to feel compassion for their patients would seem to consist at least in part in recognizing their own fears. The advantages to thinking of physician-patient relationships in largely business terms extend to patients as well: a frank discussion of bad news grows out of a genuine concern for patients. For a physician to crouch with a patient behind illusions of safety or veils of undaunted optimism would be cowardly.

What I advocate, then, is a renewed focus on the contractual element of physician-patient relationships. There are, of course, objections to the view that a physician-patient relationship is more a contract than a covenant. Those who defend the covenant model at times criticize contracts as too individualistic and at times as minimalistic (specifying only the moral minimum of the relationship). At other times, the contract model is rejected as externalistic (emphasizing external actions rather than the spirit of the relationship and the character of the agents) and legalistic (focused on legal enforcement). Those who prefer to discuss the patient-physician relationship in the language of loyalty and faith rely on virtues rather than on principles and rules. The eminent bioethicist Robert Veatch and other defenders of a contract model reply that a covenant is only a special form of contract that emphasizes moral relationships such as fidelity; they also maintain that medical ethics is best understood in terms of a broader nexus of contracts between society, the professions, and patients. Tom Beauchamp and Jim Childress

have brought this debate to life in various editions of their influential *Principles of Biomedical Ethics.*[15]

Perhaps the strongest justification for framing physician-patient relationships in terms of a covenant is that covenants seem to come down to one-sided promises between someone with power, wealth, or both and someone less powerful or wealthy. In the past 3 decades, though, legal recourse has greatly increased the power of a patient to fight a physician. The very idea of a malpractice suit impoverishes the covenant model of physician-patient relationships. That said, I have argued that patients tend to resist thinking of malpractice suits, more or less in the same way that betrothed persons resist thinking about divorce.

Although my sympathy ultimately lies with Veatch, I think that reducing relationships between physicians and patients to any single metaphor (for example, confessor, parent, friend, spouse, or expert consultant) or model will prove inadequate. The complexity of health care and the moral principles and rules that should govern such relationships compel us to think in broader terms than just contracts and covenants. We need not take a position on the debate over whether the patient-physician relationship is a covenant or a contract to conclude that the contractual dimension of the relationship can usefully offset the marriage of pity and fear Aristotle articulates.

THE ETHICS OF HOPING

The problem of many patients includes an important psychological component: illness threatens their connection to the vividness and vibrancy of the world. New medical technologies and the faith patients have in them make it easier than ever to seek to avoid the natural unpleasantness surrounding illness. Hope seems ever more rational. Physicians ought to be aware of the possible pitfalls inherent in the psychological aspects of physician-patient relationships. And those writing in the fields of biomedical ethics and medical humanities ought not to disguise or sugarcoat those pitfalls. Managing the expectations of patients demands sensitivity to their occasional delusions of control and the fragility of hope. Managing the expectations of patients requires vigilance over what Aristotle identifies as a natural tendency to indulge emotionally those we care about.

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capsule

Multivitamins should be taken early in pregnancy Research has shown that congenital heart disease is less common in infants born to mothers who took multivitamins early in pregnancy (*Am J Epidemiol* 2000;151:878-884). No risk reduction was evident when the use of vitamins began after the first month of pregnancy. The message is that periconceptional behavior is crucial to the health of the embryo.

capsule

Dying people still want to care for others Many people are not afraid of death; they are afraid of a bad death. A good death means freedom from pain and breathlessness, and clear communication with caregivers. It also means being able to contribute to the welfare of others, a new theme that emerged from qualitative research reported in *Annals of Internal Medicine* (2000;132:825-32). People who are dying are not helpless; like everyone else, they do not like to feel useless.

Medical Myth

Myth: Codeine is an effective cough suppressant for upper respiratory tract infections

Clinicians commonly prescribe codeine to reduce cough in patients with upper respiratory tract infections. The practice is now so widespread that many patients request codeine during such infections. Because most patients find coughing, particularly at night, extremely unpleasant, an effective antitussive is often desirable. Although the literature in this area is scant, some information is available, and it does not support a role for codeine in the relief of cough during these infections.

In a double-blind trial, Eccles and colleagues randomly allocated 91 patients with nonproductive cough for 6 to 96 hours to receive codeine or placebo.[1] Counts of the number of coughs were made in the laboratory for 3 hours, followed by patient-scored cough counts at home for 4 days. Patients were given 30 mg of codeine in syrup or syrup alone. During the 3-hour laboratory phase, there was no objective decrease in the number of coughing episodes. During the home phase, the result was the same. In both groups, cough decreased significantly over time, but codeine had no effect.

In a similar double-blind study by Freestone and Eccles, 82 subjects received codeine or placebo for cough associated with the "common" cold.[2] Scores of cough duration, intensity, and frequency were made. In this study, codeine was no more effective than placebo for reducing any of the variables measured.

In children, the effect of codeine is equally as dismal. Taylor and associates randomly allocated 49 pediatric patients to receive codeine, hydrocodone, or placebo on 3 consecutive nights at bedtime. Parents subjectively measured cough frequency and the effect of cough on a number of outcomes, including sleep duration. Neither codeine nor hydrocodone had an effect on cough duration or intensity in the study.[3]

Cough is an irritating symptom. Reducing cough during an upper respiratory tract infection would be a laudable goal. Codeine has been considered to be the most effective antitussive for acute cough and has been regarded as the reference drug with which the effects of other antitussive agents should be compared.[4] However, as discussed, codeine apparently does not reduce cough during such an infection. Because codeine is not only ineffective but also frequently associated with gastrointestinal symptoms, the use of codeine as a cough suppressant should be discouraged and acknowledged as a prevalent medical myth.

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PS Form 3526 September 1998 (See Instructions on Reverse)

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17. Signature and title of Editor, Publisher, Business Manager, or Owner: Business Manager — Date: September 1, 2000
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Northern California— Beautiful Sierra Foothill Community Urgent Care Clinic seeking BC/BE FP or EM physician. Send CV: Sierra Emergency Medical Group Inc., Box 4685, Sonora, CA 95370.

Academic Geriatrician: The University of New Mexico School of Medicine and the Albuquerque Veterans Affairs Medical Center are seeking two physicians (MD or DO) for the Gerontology Division, Department of Internal Medicine. Must be board certified in Internal Medicine, board eligible in Geriatrics and eligible to work in US. Position open until filled. For further information see URL: http://hsc.unm.edu./hr/jobs.html. Send inquires and CV to Robert G. Strickland, M.D., Chairman, Department of Internal Medicine, University of New Mexico School of Medicine, 2211 Lomas NE, Albuquerque, NM floor, Albuquerque, New Mexico 87131-5271. The University of New Mexico and the Albuquerque Veterans Affairs Medical Center are Equal Opportunity/Affirmative Action Employers and Educators.

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ARIZONA

All courses listed have been certified as meeting the criteria for Cat 1 of the ArMA CME Certificate and the AMA Physicians Recognition Award. To list Cat 1 CME programs, please send information to Arizona Medical Association, 810 West Bethany Home Road, Phoenix, AZ 85013; or phone (602) 246-8901.

OCTOBER 27-29, 2000: Clinical Endocrinology for Primary Care Physicians. Medical Education Resources at The Phoenician, Scottsdale, AZ. 11 hrs Cat 1. Contact MER (800) 421-3756; Fax (303) 798-5731; www.mer.org.

NOVEMBER 3-5, 2000: Scottsdale 2000 Headache Symposium. The American Headache Society at Marriott's Camelback Inn Resort and Spa, Scottsdale, AZ. 16.5 hrs Cat 1. Contact AHS (856) 423-3195; Fax (856) 423-0082; www.ahsnet.org; ahshq@talley.com.

DECEMBER 6-7, 2000: Dermatologic Procedures. The National Procedures Institute at Scottsdale, AZ. 16 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com.

DECEMBER 6-7, 2000: Sclerotherapy. The National Procedures Institute at Scottsdale, AZ. 11.25 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com.

DECEMBER 8, 2000: Flexible Sigmoidoscopy. The National Procedures Institute at Scottsdale, AZ. 6.75 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com.

DECEMBER 8-9, 2000: Orthopedics for the Office. The National Procedures Institute at Scottsdale, AZ. 12 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com.

DECEMBER 15-17, 2000: Issues in Women's Health. Medical Education Resources at The Phoenician, Scottsdale, AZ. 11 hrs Cat 1. Contact MER (800) 421-3756; Fax (303) 798-5731; www.mer.org.

CALIFORNIA, HAWAII, AND NEVADA

All courses and meetings listed are approved for Cat 1 credit toward the CMA Certificate in CME. To list accredited courses here, please send information at least two months in advance to Paulette Richardson, Continuing Medical Education, California Medical Association, PO Box 7690, San Francisco 94120-7690; or phone (415) 882-3387. For more information on accreditation or certification, please write to the above address.

ALLERGY/IMMUNOLOGY

NOVEMBER 4, 2000: Allergy Evaluation and Testing. The National Procedures Institute at Las Vegas, NV. 8 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com.

ANESTHESIOLOGY

FEBRUARY 2-4, 2001: 39th Clinical Conference in Pediatric Anesthesiology. The Pediatric Anesthesiology Foundation and Childrens Hospital Los Angeles at Disneyland Hotel, Anaheim, CA. 13.5 hrs Cat 1. Contact David J Steward (323) 669-2262; Fax (323) 660-8983.

CARDIOLOGY

OCTOBER 13-15, 2000: Coronary Heart Disease Update. MGM Grand, Las Vegas, NV. 11 hrs Cat 1. Contact Medical Education Resources, (800) 421-3756; Fax (303) 798-5731; www.mer.org.

OCTOBER 22, 2000: End-of-Life Care: EPEC With Choices. American College of Chest Physicians and The Chest Foundation at Moscone Center, San Francisco, CA. 7 hrs Cat 1. Contact American College of Chest Physicians 800 343-2227 or 847 498-1400; Fax 847 498-5460 or 847 498-8313; www.chestnet.org/CHEST/2000.

EMERGENCY MEDICINE

OCTOBER 11-14, 2000: National Emergency Medicine Board Review. Center for Emergency Medical Education at Harrah's, Las Vegas, NV. Contact CEME, (800) 651-CEME (2362) or (916) 864-4830; Fax (916) 864-4839; www.ceme.org.

DECEMBER 3-8, 2000: Maui 2000: Current Concepts in Emergency Care, 21st Edition. Institute for Emergency Medical Education and Washington Chapter of the American College of Emergency Physicians at Outrigger Wailea Resort, Maui, HI. 19 hrs Cat 1. Contact Lee Ann Williams or Lori More (800) 544-9269 or (360) 671-1800; Fax (360) 647-6008; www.ieme.com.

FAMILY PRACTICE/PRIMARY CARE

OCTOBER 8-12, 2000: Nevada Academy of Family Physicians 12th Annual CME/Golf Meeting. Nevada Academy of Family Physicians at The Rio Suite Hotel & Casino. Contact Barbara Bolling (702) 228-5822; Fax (702) 228-9737; nafplvbb@aol.com.

OCTOBER 23-26, 2000: Primary Care Update. Interstate Postgraduate Medical Association at Hyatt-Embarcadero Center, San Francisco, CA. Contact IPMA Phone and Fax (608) 231-9045; www.postgradmed.com; ipma@chorus.net.

OB/GYN

NOVEMBER 17-18, 2000: OB Ultrasound. The National Procedures Institute at San Francisco, CA. 12.25 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com

NOTICE

State Associations should send their CME listings for publication to:

Catherine Nancarrow, Editorial Manager
wjm - western journal of medicine
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San Francisco, CA 94120-7690

(415) 974-5977 · Fax (415) 822-3379
wjm@ewjm.com

CME listings can also be found on our website at www.ewjm.com/misc/CMEads.shtml

ONCOLOGY

OCTOBER 20-21, 2000: UCSF & Stanford Thoracic Oncology Conference. The Thoracic Oncology Programs UCSF and Stanford University School of Medicine at Hyatt Regency Hotel, San Francisco, CA. 11.5 hrs Cat 1. Contact Office of CME (415) 476-5808; www.som.ucsf.edu/som/education/cme/index.htm.

DECEMBER 3, 2000: CTTR 109th Semi-Annual Cancer Seminar: Soft Tissue Tumors. CTTR at Ritz-Carlton Hotel, San Francisco, CA. 10 hrs Cat 1. Contact CTTR, c/o Loma Linda University School of Medicine, (909) 558-4788; Fax (909) 558-0188; cttr@linline.com.

RADIOLOGY

OCTOBER 20-22, 2000: 2000 Symposium on Breast Cancer Diagnosis and Treatment. Stanford Radiology at Ritz-Carlton Tysons Corner, McLean, VA. 19.75 hrs Cat 1. Contact Sharon Pollio (888) 556-2230; Fax (650) 498-4335; spollio@stanford.edu; radiologycme.stanford.edu.

SURGERY

JANUARY 29-31, 2001: Colon and Rectal Surgery 2001. Keck School of Medicine, USC at the Ritz-Carlton Huntington Hotel & Spa, Pasadena, CA. 15 hrs Cat 1. Contact Registrar, USC Postgraduate Division (323) 442-2555 or (800) USC-1119; Fax (323) 442-2152 or (888) 665-8650; usccme@hsc.usc.edu.

GENERAL/MULTIDISCIPLINARY

OCTOBER 26-28, 2000: San Francisco Otology & Neurology Update - 2000. Department of Otolaryngology/Head and Neck Surgery of the UCSF School of Medicine at Renaissance Stanford Court Hotel, San Francisco, CA. 24 hrs Cat 1. Contact UCSF Office of CME (415) 476-5808; Fax (415) 502-1795; www.som.ucsf.edu/som/education/cme.

OCTOBER 28, 2000: First Regional Update of Sexually Transmitted Diseases and HIV. Sacramento County Department of Health, CARES, California Department of Health Services: STD Control Branch, UC Davis Health System and Continuing Medical Education at Hilton Hotel, Sacramento. Contact Office of CME (916) 734-5390; Fax (916) 734-8966; web.ucdmc.ucdavis.edu/edu.

NOVEMBER 1-2, 2000: EGD. The National Procedures Institute at Las Vegas, NV. 12.25 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com.

NOVEMBER 1-3, 2000: Hot Topics in Procedures. The National Procedures Institute at Las Vegas, NV. 23 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com.

NOVEMBER 2-3, 2000: Colonoscopy. The National Procedures Institute at Las Vegas, NV. 12.25 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com.

NOVEMBER 4, 2000: Flexible Sigmoidoscopy. The National Procedures Institute at Las Vegas, NV. 6.75 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com.

NOVEMBER 5-6, 2000: Medical Hypnosis. The National Procedures Institute at Las Vegas, NV. 14.5 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com.

NOVEMBER 6-7, 2000: Aesthetics Workshop. The National Procedures Institute at Las Vegas, NV. 15 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com.

NOVEMBER 10-12, 2000: Dermatology for the Non-Dermatologist. Medical Education Resources at Monte Carlo, Las Vegas, NV. 11 hrs Cat 1. Contact MER (800) 421-3756; Fax (303) 798-5731; www.mer.org.

NOVEMBER 16-17, 2000: Stress EKG. The National Procedures Institute at San Francisco, CA. 12 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com.

NOVEMBER 18-19, 2000: Office & ER Ultrasound. The National Procedures Institute at San Francisco, CA. 11.75 hrs Cat 1 equivalent. Contact NPI (800) 462-2492; Fax (517) 631-4664; www.NPInstitute.com.

DECEMBER 1-3, 2000: Managing Respiratory Diseases. Medical Education Resources at Monte Carlo, Las Vegas, NV. 11 hrs Cat 1. Contact MER (800) 421-3756; Fax (303) 798-5731; www.mer.org.

COLORADO

To list CME programs here, please send information at least two months in advance to: Mr Robert L. Kennedy, Denver Medical Society, 1850 Williams Street, Denver, CO 80218; or telephone (303) 377-1850. Brochures, course information, and registration forms are available from the contact person or organization.

NOVEMBER 6-10, 2000: 46th Annual Family Practice Review. Denison Auditorium/UCHSC, Denver, CO. Cat 1 hrs. Contact University of Colorado School of Medicine, Office of Continuing Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065.

DECEMBER 8-9, 2000: 9th Annual Bugs and Drugs. Denver Marriott Southeast, Denver, CO. Cat 1 hrs. Contact University of Colorado School of Medicine, Office of Continuing Medical Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065.

JANUARY 15-21, 2001: Neuronal & Vascular Stress: A New Window on Alzheimer's Disease. Tamarron, Durango, CO. Cat 1 hrs. Contact University of Colorado School of Medicine, Office of Continuing Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065.

FEBRUARY 10-17, 2001: CRASH 2001-Colorado Review of Anesthesia. Marriott's Vail Mountain Resort, Vail, CO. Cat 1 hrs. Contact University of Colorado School of Medicine, Office of Continuing Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065.

FEBRUARY 18-23, 2001: 27th Annual Vail Obstetrics & Gynecology Conference. Marriott's Vail Mountain Resort, Vail, CO. Cat 1 hrs. Contact University of Colorado School of Medicine, Office of Continuing Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065.

FEBRUARY 24-28, 2001: Thoracic Transplantation. Marriott's Vail Mountain Resort, Vail, CO. Cat 1 hrs. Contact University of Colorado School of Medicine, Office of Continuing Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065.

MARCH 3-10, 2001: Horizons in Surgery. Beaver Run Resort, Breckenridge, CO. Cat 1 hrs. Contact University of Colorado School of Medicine, Office of Continuing Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065.

MARCH 4-8, 2001: Neurosurgery in the Rockies. Vail Cascade Hotel & Club, Vail, CO. Cat 1 hrs. Contact University of Colorado School of Medicine, Office of Continuing Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065.

MARCH 28-April 3, 2001: AIDS Vaccines in the New Millennium. Keystone Resort, Keystone, CO. Cat 1 hrs. Contact University of Colorado School of Medicine, Office of Continuing Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065.

MARCH 28-April 3, 2001: HIV Pathogenesis. Keystone Resort, Keystone, CO. Cat 1 hrs. Contact University of Colorado School of Medicine, Office of Continuing Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065.

MARCH 29-April 3, 2001: The Molecular Basis of Neurodegenerative Disease. Sheraton Resort, Steamboat Springs, CO. Cat 1 hrs. Contact University of Colorado School of Medicine, Office of Continuing Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065.

MARCH 31-April 5, 2001: 1st Colorado Epilepsy Research Conference. Marriott's Vail Mountain Resort, Vail, CO. Cat 1 hrs. Contact University of Colorado School of Medicine, Office of Continuing Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065.

NEW MEXICO

Information, requests for accreditation, and items to be listed should be sent to the chair of the CME Committee, New Mexico Medical Society, 7770 Jefferson, Suite 400, Albuquerque, NM87109, at least two months in advance. For information on CME accreditation or on the CME requirements of the New Mexico Board of Medical Examiners, please write to the above address or call (505) 828-0237.

OCTOBER 5-7, 2000: Neurology Update. Hilton Hotel, Albuquerque, NM. Contact UNM Continuing Medical Education, (505) 272-3942.

OCTOBER 15-20, 2000: Update and Review of Internal Medicine. La Fonda Hotel, Santa Fe, NM. Contact UNM Continuing Medical Education, (505) 272-3942.

NOVEMBER 16-19, 2000: 22nd Annual Conference on Patient Education. Hyatt Regency Albuquerque, NM. Contact Society of Teachers of Family Medicine, (800) 274-2237, ext. 5415; www.STFM.org.

WASHINGTON

The listing of continuing medical education programs in Washington state is compiled by the Washington State Medical Association. To list Cat 1 programs here, please send information at least two months in advance to Continuing Medical Education, Washington State Medical Association, 2033 Sixth Avenue, Suite 1100, Seattle, WA98121; or phone (206) 441-9762 or (800) 552-0612.

OCTOBER 4, 2000: Adrian E. Flatt Resident and Fellows Conference in Hand Surgery. American Society for Surgery of the Hand at Seattle, WA. Contact ASSH (847) 384-8300; Meetings@hand-surg.org; www.hand-surg.org.

OCTOBER 5, 2000: Carpal Instability. American Society for Surgery of the Hand at Seattle, WA. Contact ASSH (847) 384-8300; Meetings@hand-surg.org; www.hand-surg.org.

OCTOBER 5, 2000: Congenital Hand Differences. American Society for Surgery of the Hand at Seattle, WA. Contact ASSH (847) 384-8300; Meetings@hand-surg.org; www.hand-surg.org.

OCTOBER 5, 2000: Cumulative Trauma. American Society for Surgery of the Hand at Seattle, WA. Contact ASSH (847) 384-8300; Meetings@hand-surg.org; www.hand-surg.org.

OCTOBER 5-7, 2000: 55th Annual Meeting - Overcoming Adversity: Hand Surgeons Shaping the 21st Century of Health Care. American Society for Surgery of the Hand at Seattle, WA. Contact ASSH (847) 384-8300; Meetings@hand-surg.org; www.hand-surg.org.

Cholera

David Heiden

Cholera ward, Wad Kowli Refugee Camp, Sudan, May 1985

David Heiden is an ophthalmologist practicing in San Francisco

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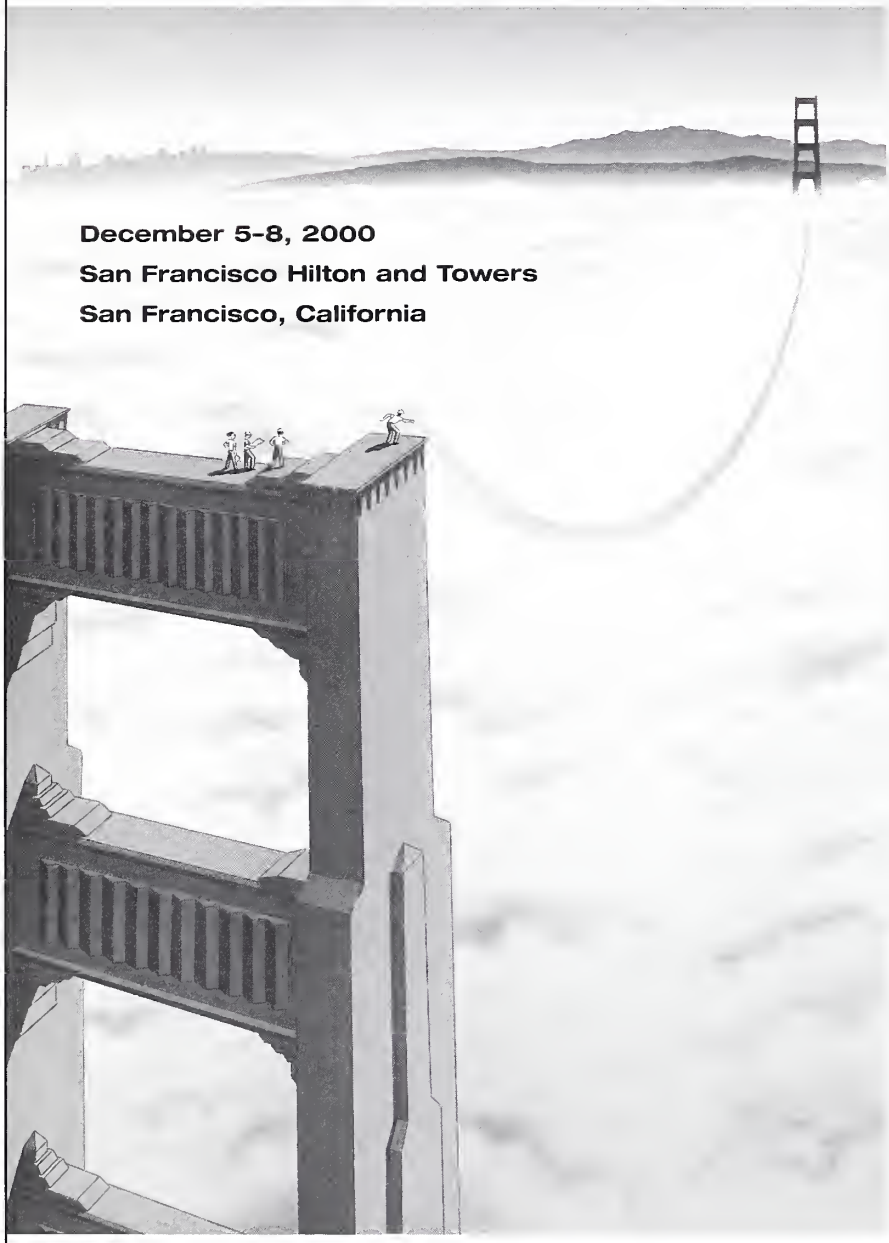

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This month in wjm

How to prevent migraine

One out of 4 households has a migraine sufferer, according to recent data from 30,000 households in the American Migraine Study. This disabling condition can lead to an impaired quality of life, and disability can be severe enough to require bed rest. But migraine headaches can be successfully prevented, says Parsekyan (p 341). Triggers should be identified and avoided if possible, and a wide range of drugs has proven efficacy in migraine prophylaxis. Beta blockers, tricyclic antidepressants, and divalproate are the first-line agents of choice.

Eating toxic mushrooms rarely causes death

Gathering and eating foraged mushrooms has become a popular US hobby, but it carries the risk of poisoning, particularly from ingesting amatoxin-containing species. But little data have been collected on the clinical outcome in cases of mushroom exposure. Nordt and colleagues analyzed data on mushroom poisoning in California from 1993 through 1997, a total of 6,317 exposures (p 314). Serious illness from poisoning was rare, and only 1 person died. The ideal management of mushroom poisoning has still not been determined, says Gussow in a commentary on p 317.

Urine screening may supersede annual pelvic examinations

Most adolescent women have had sex by the age of 19, and only about half use condoms consistently, putting themselves at risk of sexually transmitted infections. With the introduction of urine tests for chlamydia and gonococcus, argues Shafer in a Point-Counterpoint on p 293, screening adolescents with annual pelvic examinations has become obsolete. But the rate of abnormal cervical smears in adolescents, says Kahn on p 292, is high enough to warrant continued Papanicolaou smear screening of all at-risk adolescents.

Rural health care is under-resourced

Health care in the United States may be expanding—adopting new technologies and management strategies—but Rural America continues to be left behind. This month we launch a 4-part series on rural health, beginning with a look at rural provider shortages and how these could be reversed (p 348). In an Op-Ed on p 294, Ricketts argues that a comprehensive rural health care policy is needed that links resource distribution to economic forces.

Editor's pick

Perhaps there is no more important skill for a physician to develop than the effective use of the spoken word. A master physician knows not only how to use words to work miracles but how to use the unspoken word—silence—to do the same. Whereas training to harness the power and magic of verbal and nonverbal communication now begins early in medical school, it is a skill that takes years to develop fully. As with diagnosing illness or performing procedures, we can improve our communication skills if we are given regular and specific feedback. Such feedback can and should come from both patients and colleagues.

One of the skills that we need to focus on most urgently is discussing informed consent with patients. Although this concept is most often applied to obtaining permission for surgery, informed consent has a role to play in almost everything we do to patients. There is much debate about how much information needs to be provided to patients for procedures or tests that are relatively harmless, such as a blood test or a screening rectal examination. But whereas a test may be harmless, a false-positive result can lead to additional workup that may be far more invasive than the original test.

Even if such testing is not invasive, a false test result—either false-positive or false-negative—can cause unnecessary psychological worry. In this month's *wjm*, Schwartz and colleagues investigate whether women's understanding of false-positive mammographic results influences their interest in being screened for cancer (p 307). Their most interesting finding is the high acceptance rate women have for false-positives—nearly 40% would tolerate 10,000 or more false-positive test results leading to a biopsy for a single life saved. This high acceptance of false-positives should not diminish our determination to provide fully informed consent, but it should alert us to the faith that the public has in technology and the value placed on saving a single life.

The accepted norm in contemporary society is to share bad news honestly and openly with patients, and physicians are now trained to break bad news. But truth and honesty may not always represent a clear "best choice." What of telling demented patients the truth about their illness? Marzanski brings us to a more complete understanding of the advantages and disadvantages of truth-telling in caring for this complex illness (p 318).

Communication skills are of paramount importance in all specialties and practice environments. This issue of *wjm* provides food for thought to those of us struggling to understand how to provide the best information to our patients.

wjm

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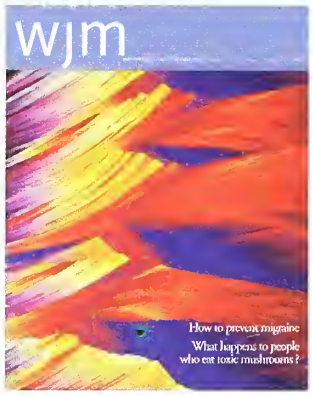

Michael W Davidson/The Florida State University

Photomicrograph of diltiazem, a second-line agent used in migraine prophylaxis

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Point-Counterpoint

With urine-based screening, do sexually active adolescent girls still need annual pelvic examinations?

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2000;173:292

Yes: Pelvic examination continues to play a key role

The pelvic examination is a fundamental component of reproductive health care services for sexually active adolescent girls. Those who propose that routine pelvic examinations are now unnecessary—because infection with *N gonorrhoeae* and *Chlamydia* can be diagnosed using urine specimens—are overlooking several issues critical to young women's health.

First, external genital and speculum examinations are often required to diagnose asymptomatic sexually transmitted infections. Adolescents frequently do not recognize signs and symptoms of genital herpes, condylomata, and syphilis, which may present as vulvar, vaginal, or cervical lesions. Trichomoniasis causes substantial morbidity but is often asymptomatic and requires a vaginal swab for diagnosis. Insufficient data exist regarding the quality of self-collected specimens in adolescents, and many adolescents are intensely uncomfortable self-inserting a swab. If these infections go undiagnosed, a crucial opportunity to provide prevention counseling, treat infections, and prevent transmission to sexual partners is missed.

Science Photo Library

Colored transmission electron micrograph of human papilloma viruses

Second, a speculum examination is necessary to obtain a Papanicolaou smear. Human papillomavirus (HPV) infection is highly prevalent in adolescents.[1] Many adolescents who were infected at a young age through vertical transmission or sexual abuse are at risk for cervical dysplasia, and the overall prevalence of abnormalities on Papanicolaou smears is as high in adolescent as in adult women and is probably rising.[2,3] Instead of discontinuing cytologic screening, we should develop primary prevention initiatives and innovative strategies that enable providers to predict which adolescents are likely to develop progressive cervical dysplasia so as to avoid unnecessary Papanicolaou smears and colposcopy.

Third, the pelvic examination provides a valuable opportunity to educate adolescents about their reproductive anatomy and to teach and reinforce preventive gynecologic health care practices that may prevent morbidity and mortality throughout life. Trusted primary care physicians are in the optimal position to provide this education. Although the examination engenders embarrassment and fear in some adolescents, this certainly does not justify not performing an important preventive health service. Instead, we should focus on teaching health care professionals the communication and technical skills necessary to demonstrate respect and perform a comfortable examination.

Many medical organizations dedicated to adolescent and young women's health have developed guidelines stating that sexually active adolescents should receive routine pelvic examinations. The recommendation to eliminate them sends the harmful message that we do not value reproductive health care services for adolescent girls. Instead, we should be advocating strongly for the specific needs of adolescent girls in current debates about the allocation of preventive care resources.

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No: Recommending annual exams is not evidence based

Two of every 3 adolescent girls in the United States have had sexual intercourse by age 19, and most use condoms inconsistently, placing themselves at risk of sexually transmitted infections and unintended pregnancy. Rates of chlamydia and gonorrhea are 6 times greater in this age group than the national average. Most of these infections are asymptomatic, making screening an essential technique for infection control. Human papillomavirus infection is the most common sexually transmitted infection in this population and has been linked to an increased risk for the development of carcinoma of the cervix.

Based on this risk, and the ability to screen for cervical carcinoma by Papanicolaou smears, a number of distinguished professional organizations—such as the Institute of Medicine and the Centers for Disease Control and Prevention—recommend annual pelvic examinations as soon as a young adolescent becomes sexually active. However well-meaning, these recommendations are not evidence-based but were developed mostly by committee consensus.

Cervical cancer is a rare event in adolescents. The tumor registry in California reports that it would take 500,000 pelvic examinations with Papanicolaou smears to identify 1 cervical carcinoma in this age group. This low rate of cancer in adolescents is supported by the most recent review of smears in teens in which not 1 case of carcinoma was identified among more than 10,000 smears reviewed.[1] The largest review of smears in sexually active teens and young adults reported a low rate (1.9%) of squamous intraepithelial lesions (SIL).[2]

Most cytopathologists now agree that low-grade SIL represents infection with the human papillomavirus and that the infection will resolve within 24 months.[2] In most cases, the cytologic changes revert to normal. Thus, an aggressive interventional approach to low-grade SIL, including colposcopy, is no longer widely accepted.

If cancer is not prevalent in this population, and if a commonly diagnosed condition—low-grade SIL—resolves in the vast majority of patients, we clearly need to reassess the annual Papanicolaou smear program. There are intangible but real costs of falsely abnormal ("false-positive") changes on smears: young women can become overly worried about developing cancer and may have to undergo repeated examinations unnecessarily.

Trek Diagnostic/PR News Foto

Urine culture systems can be used in the diagnosis of gonococcal and chlamydial infections

Sexually transmitted infections, rather than cervical cancer, pose a more immediate threat to adolescents. Accurate urine screening tests are now available for chlamydial and gonococcal infections, and screening for chlamydia is cost-effective,[3] making annual pelvic examinations for healthy adolescents obsolete. Continuing with the current recommendation for annual screening for sexually transmitted diseases, but now substituting the new urine-based technologies, the challenge before us is to determine which young women need a Papanicolaou smear, when should screening begin, and how often should it be done.

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Op-Ed

Health care in rural communities

The imbalance of health care resource distribution needs correction

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West J Med
2000;173:294-295

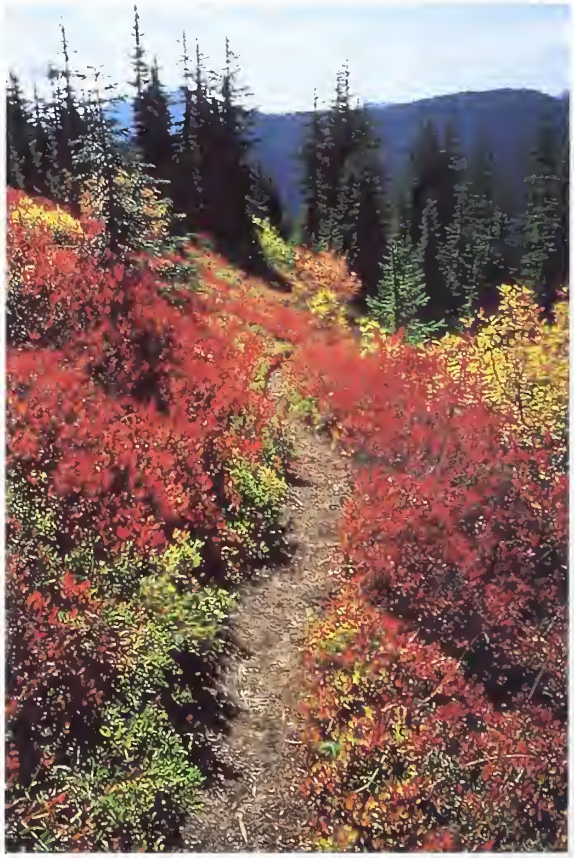
The rapid pace of change in health care delivery in the United States has touched all parts of the nation, including small and rural communities. Rural people have been affected by the revolutions in financing, from fee-for-service to managed care; in the use of technology, where treatment is now data-intensive; and in the relationships between patients and professionals, where there are more options and greater expectations of quality and accountability. However, these changes have not affected rural communities in the same way they have affected more central and populous places. Rural people may not be getting their share of the benefits of medical progress and the new structure of health care.

The health care systems of urban America have expanded at a pace reflected in the percentage of the economy dedicated to medical care: from 8% of gross domestic product in 1980 to 13.5% in 1998.[1] This growth has not been matched in rural communities because the most important components of that growth—the highest and newest technology, the expansion of systems to monitor and track care-giving and costs of care, and the entry of new types of professionals and institutions into the field—have all occurred largely in urban areas. Rural America remains relatively under-resourced in health care. Many rural communities continue to experience shortages of physicians; as of midyear 2000, 1,182 non-metropolitan areas or populations were designated as Health Professional Shortage Areas (HPSAs) (US Dept of Health and Human Services, unpublished data, 2000), and 36.8% of all rural hospitals lost money compared to 32% of urban hospitals under financial strain.[2]

A series of articles that are launched in this issue of *wjm* and are based on the book *Rural Health Care in the United States*[3] describe the comparative characteristics of the rural health care delivery system. The series and the book make the case that rural America has indeed been left behind. If managed care was to bring discipline to the health care market and encourage innovation through competition, then rural places lost that positive effect because managed care companies largely ignored rural markets. Rural health care changed more as a result of the increased integration and assimilation of professionals and institutions into systems and networks than in the way in which health care is financed. Indeed, comprehensive relief legislation focusing on rural health care has been introduced in Congress in 2000. Special programs and policies, such as the Rural Hospital Flexibility Program, which was part of the Balanced Budget Act of 1997, and the Rural Outreach and Rural Networds grant programs have been implemented to cope with the imbalance of major payment programs such as Medicare.

Primary care physicians are an important resource for rural health care. But the distribution of physicians remains skewed toward urban areas: rural America has 20% of the nation's population, but less than 11% of its physicians.[3] This imbalance has become worse over time. In 1980, the percentage of physicians practicing in non-metropolitan counties was 13.6%, but it had fallen to 12% by 1990. The total supply of patient care physicians grew by 24.3% between 1990 and 1997, but by only 11.1% in non-metropolitan areas.

The programs that attempt to address the distribution of professional resources and support direct care have been successful up to a point, but they run against a tide of stronger forces that draw capital, people, and services into central places—the cities—and away from rural areas. In a sense, the imbalance of health care resources between rural America and the remainder of the nation is a "condition." That is, it is a persistent characteristic of the system. We describe it, however, as a "problem," which should, as



Douglas Dickema

John Kingdon explains in his classic work on policy, attack solutions, even from what he calls the policy "garbage can."[4]

The trouble is that these solutions address the symptoms rather than the fundamental causes of rural disparities. More than one commentator has noted that the United States does not even have a "rural policy," much less a rural health care policy.[5] But only a comprehensive policy, one that links health care resource distribution with underlying economic forces and overall economic planning, can deflect or reverse the factors that cause the imbalance. But the United States has no such policy, a fact that individual states are learning as they attempt to bring the rural regions into the twenty-first century.

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The risks of having children in later life

Social advantage may make up for biologic disadvantage

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When is the best time in life to be a mother? Or a father? These questions have been raised in the past, but the answers have left uncertainties. To address some of these issues, Nybo Andersen et al, in a study looking at maternal age and fetal loss, used a large set of data from three linked Danish health registries.[1] A digest of their original paper appears on p 331 of this month's *wjm*. Their findings are largely confirmatory of what is known or has been suspected: older age strongly increases a woman's chances of at least three untoward outcomes, namely stillbirth, miscarriage, and ectopic pregnancy. However, prospective parents concerned about their age may hope for answers to other questions as well.

Over the past 50 years or so, options for controlling or enhancing fertility have grown. These changes began with the introduction of oral contraception and have continued with the legalization of induced abortion and the development of ever more sophisticated techniques of in vitro fertilization and advances in obstetrics that ensure safe deliveries. Older women especially benefit from all of these for each has increased the age at which women bear children.

For instance, the Danish tables show trends in the rates of induced abortions over the period 1978-1992. On one side of the reproductive age span, these occur proportionately most frequently during the teens, when the greatest social disadvantage is associated with childbearing. On the other side, the greatest number, proportionately, of induced abortions occur at the latest ages, when the greatest biologic disadvantage is associated with childbearing.

The collection of such large bodies of data often limits the social and biologic variables that can be recorded. Still, the data reported by Nybo Andersen et al could have been stretched further. For example, they provide a mean length of gestation for miscarriages rather than a distribution over the range of specific gestational ages. Such an analysis obscures the relation between miscarriages at different stages of gestation and maternal age.[2] The greatest concentration of chromosomal anomalies and by far the highest rate of pregnancy loss is found early in gestation. At least 90% of such losses occur during the first trimester. At the same time, those anomalies that are trisomic and those fetuses that are less viable are strongly related to increased maternal age.

It may also not be asking too much of routine data on stillbirths to differentiate between antepartum and intrapartum losses. In recent years in developed countries most losses occur before labor, and only in these is the effect of maternal age observed.[3] Hypotheses about the causes of antepartum stillbirths occurring at advanced maternal age have included chromosomal anomalies, pre-eclampsia (especially in nulliparous women), and diabetes. None of these factors, however, contributed to the age effect observed in a large data set on stillbirths in Canada collected from 1961 to 1993.[4] Unlike the Danish series, the data in this perspective, obtained over a longer time, did show a considerable decline in the overall rate of stillbirths. It is also notable that older mothers shared in this general long-term decline in the rate. Thus, among women aged 35 years or older, the rate of stillbirths per 1000 births decreased from 16.5 in 1960-1969 to 5.8 in 1990-1993. Though the higher relative risk for older women persists, the absolute risk has been greatly reduced.

Maternal age has an impact on other aspects of reproduction for which information may not have been available in the Danish register. Among the data that are usu-

ally recorded are multiple births and congenital malformations. Delayed conception or infertility, although certainly of interest, will often not be recorded.

The incidence of multiple births increases with the age of the mother, but distinctly more so for dizygous rather than for monozygous twins and more so still for triplets.[5] In recent times, however, infertility treatment has increased the rate of all multiple births, and this surely confounds the effects of natural age.

When birth defects are considered, children born of older women have a consistently increased risk only for Down's syndrome, which is less of a hazard now than it was, owing to the advent of prenatal screening. Not as well known is the fact that certain rare disorders, such as achondroplasia, are more common among births to older fathers.[6] Some of these disorders, presumed to be new mutations, are detectable in offspring only later in life; schizophrenia is one example.[7,8]

PARENTAL AGE AND INFERTILITY

Information on parental age and infertility, which is usually beyond the scope of routine records, is important in advising prospective parents. Thus, Nybo Andersen et al, like other authors, provide estimates of fetal loss occurring between the time a pregnancy is recognizd and a live birth.[1] But in addition to fetal loss, older couples are more likely to have subfertility or infecundability (failure to conceive). If a recognized pregnancy occurs, the simple recording of the "time to conceive" yields a relative measure of fecundability. Although it is beyond the scope of routine records, studies that have used highly sensitive human chorionic gonadotrophin tests to look at very early pregnancy have helped to distinguish between an absolute failure to conceive and loss before the first missed period.[9] Older women do worse in both respects.[10] However, when oocytes are randomly assigned to women of various ages during in vitro fertilization procedures (in which the uterus is hormonally prepared), embryos implant equally often among women older than 40 and among younger women. Still, older women are less successful in sustaining an embryo.[11] Outside the experimental situation, age carries the added risk of a trisomic oocyte. Thus in real life, the older woman carries two independent risks: conceiving a trisomic oocyte and having a less efficient uterus. Neither of these risks is an absolute bar to childbearing; successful pregnancies do occur, if seldom, up to age 45 or older.

Typically, menstruation and ovulation cease with menopause at around age 51 or 52. Yet women in their late 40s seldom conceive and complete a pregnancy without the assistance of modern techniques. Classic studies in populations that do not use contraception, such as the Hutterites, show that childbearing declines steeply as women pass into their 40s, well before menopause.[2]

The reasons for this decline in fertility as a woman ages relate to both the oocyte and the uterus. Although the oocyte becomes increasingly vulnerable with age, remarkable technical advances have substituted for failing physiologic nurture of embryos. When embryo replacement was first achieved, women aged over 35 were seen as poor candidates for the procedure. Now with better hormonal control, older women are often successfully treated.

THE ADVANTAGES OF HAVING CHILDREN IN LATER LIFE

Finally then, after potential parents have weighed the age factor in terms of conceiving and carrying a pregnancy to term, they may be comforted to know that a child born to older parents does have advantages. In some studies that have controlled for social factors and parity, such children do better at school than those of very young parents.[12,13] In the demanding task of raising children, older parents may be less resilient than younger ones, but their experience and knowledge are almost bound to be greater, their economic situation better, and child rearing more affordable. Biologic disadvantage is to a degree balanced by social advantage.

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In the Public Eye

News and Features

Short, sharp bouts of exercise good for the heart

Scott Gottlieb, New York

Two new studies offer some good news and some bad news about exercise, especially for people who are just starting. Shorter bouts of exercise can be just as effective at protecting the heart as longer workouts, but getting the heart rate up is a key factor because light activity offers no cardiac benefit.

Physical activity has long been associated with a decreased risk of coronary heart disease. It has been unclear, however, whether the duration of exercise episodes was important and whether accumulated shorter sessions were as predictive of decreased risk as longer sessions, provided that the same amount of energy was expended in each instance.

In 2 new studies, the researchers found that even with relatively small amounts of physical activity, with an energy expenditure of only 1,000 kcal (4.2 MJ) a week, the risk of coronary heart disease decreased by 20% compared with that in people who did not partake in that amount of activity. Whether the exercise occurred in a few long sessions or more frequent shorter sessions did not matter—there was a positive correlation between lowered risk and vigorous activity.

The same group of investigators conducted both studies, exploring the effects of the intensity and duration of exercise on coronary heart disease. Data for the 2 studies were taken from the Harvard alumni health study, during which Harvard alumni who entered the university from 1916 to 1950 were observed (*Circulation* 2000;102:975-980, 981-987).

In the first study, led by Dr Howard Sesso from the Department of Epidemiology at the Harvard School of Public Health in Boston, the researchers observed 12,516 men aged 39 to 88 years from 1977 to 1993. They found that those who expended more than 1,000 kcal a week in total physical activity reduced their risk of coronary heart disease by about 20%.

Overall, a lower but nonsignificant reduction in risk of 10% was seen for those expending 500 to 999 kcal a week, slightly less than the current exercise recommendations of the US Surgeon General.

In addition, the researchers found that vigorous activity was also predictive of a reduction in risk. "Moderate and light activities, which may be less precisely measured, showed nonsignificant inverse association," the article said. The subject's heart rate needed to be raised more than 75% above baseline, so if a person's heart rate was 60, he or she needed to raise it above 105.

In a second study, led by Dr I-Min Lee from the Department of Medicine at Brigham and Women's Hospital and Harvard Medical School in Boston, the researchers again found that physical activity was associated with about a 20% decrease in the risk of coronary heart disease.

This study observed 7,307 men with an average age of 66 years from 1988 to 1993. The researchers found that shorter sessions of physical activity were just as beneficial in decreasing the risk of coronary heart disease as 1 longer, continuous session of exercise, as long as the total caloric expenditure was equivalent.

Scooters cause 9,500 injuries in US in 8 months

Deborah Josefson, San Francisco

A sharp rise in injuries related to using foot-propelled scooters is leading to an increased demand that children using them should wear mandatory protective gear. The US Consumer Product Safety Commission has reported that emergency room visits from

Lee Marmer

Most scooter accidents occur in children aged 15 years and younger

scooter-related mishaps are up 700% since May. In all, 9,500 injuries have been reported so far this year, with over 4,000 of these reported in August alone.

Most scooter accidents have occurred in children aged 15 years or younger; fractures account for 30% of the injuries.

Scooters have become enormously popular in the United States, Europe, Hong Kong, and Israel; both children and adults can be seen using them in crowded cities. The current models are updated versions of their 1950s predecessors and feature lightweight, foldable metals such as aluminium or titanium, narrow bases, and low friction wheels similar to those used in in-line skates. Most models weigh less than 4.5 kg, cost $80 to $120, and are portable.

Most injuries in scooter riders are sprains, but fractures and dislocations accounted for almost a third of the reported mishaps. Head injuries also occur. So far, no deaths have been reported.

Compared with the number of injuries from in-line skating and skateboarding, which amounted to 100,000 and 60,000, respectively, in 1999, those reported in scooter riders seem low. However, this may just reflect a catch up period; in 1992, when in-line skating first became popular, the Consumer Product Safety Commission collected only 10,000 reports of in-line skating accidents.

The commission is recommending that children who use scooters don full safety gear, including helmets, knee pads, and elbow pads. Additionally, they recommend that users adhere to well-paved surfaces and avoid street traffic. Children aged 8 years and younger should not use scooters without supervision, and using them at night should be avoided, said the Consumer Product Safety Commission.

Ann Brown, the commission's chairwoman, commented: "We're trying to head off some of the kind of injuries that happen with in-line skates and let people know about the safety gear early on." Some states are proposing that children on scooters wear bicycle helmets.

Meanwhile, legislation to ban motorized versions of the scooters have been drafted in Colorado, and such scooters have been prohibited in New South Wales, Australia.

Patients may gain access to doctors' disciplinary data

Deborah Josefson, San Francisco

Patients in the United States may soon be able to access currently protected information about their doctors, including malpractice data, if a bill introduced through Congress is passed.

Representative Tom Bliley (R-Va), chair of the House commerce committee, spearheaded controversial legislation that allows the public to have access to the National Practitioner Data Bank. The legislation enters delicate territory, where it is important to balance consumers' right to knowledge and physicians' right to privacy and protection against libel.

The data bank was set up by Congress in 1986. Its aim was to facilitate both peer review and the process for licensing physicians. Access to the database has been limited to hospitals, insurance companies, state medical boards, and physicians seeking information about themselves.

Currently, the database collects information such as adverse disciplinary actions taken by state medical and dental boards, suspensions of clinical privileges by hospitals, medical malpractice liabilities, exclusions from participating in Medicaid and

Linda Spillers

Tom Bliley is spearheading the controversial legislation

Medicare programs, and actions taken by the Drug Enforcement Agency against the practitioner.

In the United States, physicians who lose their license in 1 state can cross state lines and practice in another state. The data bank allows states to find out if a license to practice has been revoked by another state and thus facilitates the licensing process. Although access to the bank is restricted, more than 30 state medical boards allow consumers to query them on the status of doctors practicing in their states.

The drive to make the national database public comes on the heels of several well-publicized examples of disturbed or incompetent doctors who were still practicing medicine. Chief among these was the case of a respected neurosurgeon who operated on the wrong patient and removed healthy instead of tumor tissue. Another case was that of Dr Alan Zarkin, an obstetrician and gynecologist, who carved his initials on a patient's abdomen after performing a cesarean section. He continued to practice for 5 months afterward, despite dismissal from the staff of the hospital where the incident occurred.

Proponents of a public database argue that it will allow consumers to make more informed decisions when choosing their doctors. Physicians' groups, such as the American Medical Association and the American Osteopathic Association, however, point out that the information in the database is useless for this purpose because it is out of context.

Three quarters of the information in the data bank concerns malpractice suits. Malpractice information can be misleading because the number and size of settlements do not necessarily reflect a physician's competence.

Moreover, a recent study in *The New England Journal of Medicine* found that only 1 in 5 malpractice suits is settled with an admission of the physician's negligence. Insurance companies often settle suits to avoid costlier court cases, and thus, the mere existence of a suit or settlement does not reflect the merits of the litigation.

Physicians in high-risk specialties, such as surgeons and obstetricians and gynecologists, or those who take on sicker patients and conduct cutting-edge clinical research, may also face higher malpractice rates than the average general practice doctor. Consumers who screen out such physicians on the basis of a high number of suits deprive both themselves and the doctors, the organizations say.

An Associated Press review of the data bank earlier this year found about 500 physicians and dentists who had been slapped with at least 10 disciplinary actions or malpractice suits in the past decade. After that, the *New York Daily News* featured several of these physicians in a front-page article.

In a Congressional hearing on the matter, Dr Charles Norwood, a surgeon and member of Congress, voiced his concerns: "Making the National Practitioner Data Bank [NPDB] public is an asinine idea because it attaches a level of sophistication to the database which is not appropriate and ignores state-based approaches that make more sense and are already in place today. The NPDB is simply gathered information. It has no context. Information does not in any way explain the conditions behind judgments made in specific cases."

Others are concerned that if the data bank is made public, doctors will be discouraged from self-reporting their errors and those of their peers.

Despite these concerns, efforts to open the bank continue. Congressman Bliley hopes to model the public version on the Massachusetts Physician Profiles project that allows consumers access to information about physicians' malpractice suits and criminal actions (www.massmedboard.org) and to push the bill through Congress before the end of the year.

capsule

Research on race must use justified definitions Editors at the *Canadian Medical Association Journal* (2000;162:1393) urge researchers to stop using meaningless descriptors such as "black" and "white" when describing the participants in their research. Unsophisticated references to race are biologically unsound and unlikely to be relevant to the research question, they say. Use of all ethnic descriptors must be scientifically justified and clearly explained.

Media Watch

HIV disinformation

Gavin Yamey
Deputy editor, *ujm*

If you telephone the San Francisco office of the HIV campaign group Act Up (the AIDS Coalition to Unleash Power), an answer phone message announces 2 surprising "facts." First, "HIV cannot possibly cause AIDS." Second, "AIDS drugs are poison." The San Francisco group, joined by branches in West Hollywood, Toronto, and Atlanta, is on a crusade to challenge what they see as the medical establishment's intellectual stranglehold over the AIDS community.

Their crusade took on a high profile recently with a flurry of media interest in the author Christine Maggiore. *Newsweek* called her "the HIV disbeliever." In her book, *What if Everything You Knew About AIDS Was Wrong?,* she explains that HIV tests are unreliable, pregnant women who are HIV-positive cannot transmit the virus to their babies, and AIDS is not a global health problem. Maggiore was 1 of the "HIV dissenters" invited to meet the South African president Thabo Mbeki at this year's 13th International AIDS Conference in Durban, South Africa. Act Up San Francisco recently took up her cause, inviting her to a public meeting to discuss "the truth" about AIDS in Africa.

This was no ordinary meeting. Outside the hall, activists wandered around in T-shirts that declared "Warning! This area is being patrolled by Act Up." They handed out leaflets saying, "Don't Buy the HIV Lie." The group is famous for its direct-action activities, and wherever they go, they inspire the feeling that something unsettling is about to happen.

Maggiore proved to be an eloquent and calm spokesperson. Although her views may be extreme and often untenable, she does not come across as an extremist when she recounts her own experiences. She described that in 1992, doctors told her that she was HIV-positive. She had another test that was indeterminate, then a negative test, and finally another positive test. This uncertainty led her to question the scientific knowledge about the virus and the disease, and she then set up Alive & Well AIDS Alternatives, a nonprofit organization "founded by HIV-positives who have learned to live in wellness without AIDS drugs and without fear of AIDS." Her personal choice is perhaps understandable, if unconventional.

But when she started to talk about Africa, her beliefs began to sound increasingly bizarre. HIV disease is not a problem in Africa, she explained, and the figures for the number of infected people are simply false. The sick and dying people she saw in the hospitals could not have had AIDS. "Poverty," she said, "malnutrition, and lack of access to basic medical care were causing the devastation and disease."

At this point, Maggiore's partner, a film director, showed the audience a film he made when he accompanied her to Durban. We hear a South African journalist saying, "I'm scared for Africa and where it might go. The only hope is Thabo Mbeki." We see a young HIV-positive man who has stopped all of his antiretroviral medication. "I don't have fear," he says. "Fear is a terrible emotion."

It is hard to make sense of all this HIV disbelief, but these 2 voices in the film give some clues. AIDS has been a catastrophic illness, decimating the gay communities in San Francisco and Sydney, Australia, and now is ravaging the developing world. The United Nations estimates that 1 in 2 teenagers in Africa will develop the disease. How is it possible to deal with this appalling phenomenon? Perhaps by denying that there is a problem at all. Boston college psychology professor Joseph Tecce, who has studied AIDS dissenters, told *Newsweek*: "The basis of denial is a need to escape something that is terribly uncomfortable. If something is horrific, I might want to pretend it doesn't exist."

At the end of the meeting, Maggiore took questions from the audience, and the atmosphere turned confrontational. One man screamed at her to "read MEDLINE" for the wealth of evidence about HIV and its treatment. Another explained that his HIV-positive friends had responded well to combination therapy and that they had no intention of throwing away their drugs.

The international scientific and medical community has made it clear what it thinks of dissidents like Maggiore. More than 5,000 scientists have now signed the Durban Declaration (http://www.durbandeclaration.org), which states: "The evidence that AIDS is caused by HIV-1 or HIV-2 is clear-cut, exhaustive and unambiguous. This evidence meets the highest standards of science." The signatories say, "It is unfortunate that a few vocal people continue to deny the evidence. This position will cost countless lives."

Other HIV activists in the United States and the developing world, including Nobel Prize winners Doctors Without Borders, are similarly outraged by the dissidents. These activists are campaigning for the fundamental right of people in poor countries to have access to HIV medicines. When Maggiore says that poverty is killing Africa, this, they believe, is only a half-truth. Lack of medicines is equally as deadly. The activists publicized their anger at a rally in Durban, carrying placards that read, "One Dissenter, One Bullet."

The 4 rebel Act Up groups want people to reexamine the orthodox view of AIDS. But if this leads to people abandoning the use of safe sex, have they really done the world a service? The number of new HIV cases in San Francisco has risen recently, so people cannot afford to be complacent. Maggiore's mantra, uttered again and again at the Act Up meeting, is that "you have a choice" in whether to take treatment. Perhaps she should tell that to the 24 million people living with HIV and AIDS in Sub-Saharan Africa.

Media Watch Update

AIDS activists target "renegade group"

ACT UP/San Francisco is a "renegade group" that discourages testing for the human immunodeficiency virus (HIV), disrupts informational meetings on HIV/AIDS, and "commits communitywide medical malpractice" by disputing the need for HIV medications, the San Francisco-based group, AIDS Activists Against Violence and Lies, wrote in a *San Francisco Chronicle* "Op-Ed" piece (D Wohlfeiler, S Lew, and H Wilson, September 21, 2000, p A27).

The activist group sponsored full-page ads, listing 5 organizations and 194 individual signers, in the local gay press. The group also held a press conference on the steps of City Hall, calling on the community to boycott ACT UP/San Francisco.

Rebecca Hensler, who helped found ACT UP/San Francisco but left when the current leaders took over, said, "[Their message] is threatening the city's ability to provide support services and medical care for people with HIV. The community has had enough" (C Heredia, *San Francisco Chronicle,* September 22, 2000, p A21). Survive AIDS' Michael Lauro, who is coordinating the campaign, said, "I sense a commitment, finally, within our community to confront [ACT UP/San Francisco's] violence and their violent message" (U Torassa, *San Francisco Examiner,* September 21, 2000, A20).

Activists speak out

AIDS Activists Against Violence and Lies contend in their editorial that ACT UP/San Francisco promotes the "myth" that HIV does not cause AIDS and uses the slogan "AIDS is over" on its Web site and bumper stickers. They claim that the group is using the name of another organization, ACT UP—which was founded in the 1980s and is dedicated to increasing resources and treatments for HIV/AIDS—to "appropriate the original['s] . . . credibility." While acknowledging the group's "right to believe what they want," the authors "will not accept that even one potential volunteer becomes afraid to get involved, or worse, that one infection takes place, due to ACT UP/San Francisco's tactics."

The activists conclude, "It is time for all San Franciscans, and all of us fighting AIDS, to stand together and declare our commitment to respect, dialogue, and a healthy future for all of us" (*San Francisco Chronicle,* September 21, 2000, p A27).

ACT UP/San Francisco replies

Members of ACT UP/San Francisco contend that there is "little to fear from the new effort." Michael Bellefountaine, who considers the new group (AIDS Activists Against Violence and Lies) part of the "AIDS industry," said, "These are the people who told us that protease inhibitors were the cure, and it's no wonder they are rallying around to suppress our message."

David Pasquarelli, an ACT UP/San Francisco member who tested positive for HIV in 1995, said, "The issue is not our tactics; it's our message that HIV does not cause AIDS, and the drugs they are pushing are costing countless lives" (*San Francisco Chronicle,* September 22, 2000, p A21).

Adapted from California Health Care Line, with permission from California Health Care Foundation

Medicine and Money

Human tissue for sale: what are the costs?

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Several academic hospitals in the United States are forming partnerships with biotechnology companies to provide human tissue for use in research, treatment, or drug development. This series of arrangements raise wide legal and ethical issues. Harvard University's Beth Israel Deaconess Medical Center in Boston, Massachusetts and the Duke University Medical Center in Durham, North Carolina are among the latest academic hospitals to form partnerships with biotechnology companies for the purpose of providing human tissue for use in research, treatment, and drug development. Both of these institutions have entered into agreements with Ardais, a genomics startup company, which will bank the tissue, collect data, and sell both the data and the tissue to interested parties. Patients undergoing surgery at these medical centers will be asked to sign permission forms that enable the medical center to send leftover pathology specimens to biotechnology companies.

© Bill Denison

David Lacks holds a portrait of his mother, whose cells have been used without permission

Ardais intends to create a massive tissue catalogue, allowing researchers to place Internet orders for tissue samples from patients with the specific diseases they are studying. The company will maintain the confidentiality of patients by assigning a numeric code to the donated tissue and clinical information so that medical researchers will not be able to contact the patient.

Although there is a great need for centralized, data-linked tissue banks, and surplus tumor tissue is usually discarded anyway, such partnerships raise interesting ethical, financial, and legal questions. Chief among these concerns are issues of privacy, the commodification of body parts, and whether there is any financial or moral obligation to compensate the tissue donors for contributing the raw material for research and development.

Tissue donors, because of the anonymous nature of the donation, may not see any medical or therapeutic benefit from the donation. Will cash-strapped hospitals be tempted to enter into these agreements in order to buttress their financial status?

Tissue banking and joint academic and industrial ventures are not new, but awareness of some of the legal, financial, and ethical implications that they raise is. Many academic hospitals routinely bank frozen tissue of rare and interesting tumors. Usually these tissues are studied in-house as a means to aid in diagnosis, and often the tissue is shared with researchers from other departments and hospitals. Increasingly, shrewd or misguided patients request that their tissue be sent to a company involved in in vitro tissue chemotherapy sensitivity testing or genetic testing.

The biomedical community also has a legacy, however, of using such tissues without the patient's the knowledge. Often, these uses begin innocently, such as in an attempt to investigate disease, but even then ethical considerations arise. Henrietta Lacks, for example, was a poor, young woman who died of cervical cancer in 1951. When she was a patient at Johns Hopkins Hospital in the early 1950s, a sample of her cervical cells was sent to an in-house researcher who was trying to grow human cells in culture. Although Ms Lacks died nearly 50 years ago, her cells continue to live on as the HeLa cell line. They have contributed to countless biomedical discoveries and can be ordered from tissue culture supply catalogues. Despite this contribution to scientific exploration, neither she nor her family gave permission for these cells to be used, and the family was never compensated for any profits made from them.

Public policy regarding tissue donation and use is confused. Trafficking of vital or-

gans for profit is illegal and is specifically proscribed under the National Organ Transplant Act of 1984. When it comes to other tissues, however, the rules are hazy. Officially, sales of other tissues are also illegal, but tissue banking is big business and the law is readily sidestepped by invoking "processing and handling fees" so that the tissue itself is not officially sold.

Profit-making tissue banks have been the beneficiaries of increased organ donations. According to the American Association of Tissue Banks, tissue donation has increased by 172% in the past 5 years. This increase is largely due to the fact that such organisations are informed when a patient dies.

In the United States, when a patient dies in a hospital or nursing home, doctors must ask if the family consents to organ and tissue donation. This action is mandated by the National Organ and Tissue Donation initiative of 1999. Whereas vital organs have a finite life span and must be transplanted within hours, tissues such skin, corneas, tendon, bone, and heart valves can be harvested later and cryopreserved. Thus, more tissues than organs are donated. A good proportion of these body parts are processed and sold for profit and become such items as bone putty and collagen. The tissue donor's family is usually not aware of the destination of the body parts and is not financially compensated—nor is it clear that the family should be. Many believe that the transplant and donor pool would shrink if the public realized the commercial potential.

The commodification of body parts and the widening of the gap between rich and poor, with the poor selling their tissues, is also a repugnant scenario. Interestingly, donors have long been able to sell their blood, sperm, and eggs in the United States, perhaps because these are seen as self-replenishing or surplus body parts.

Clearly, a bank of human tissues is needed to enable further research, diagnosis, and therapeutic development. The ability to relate the molecular findings of the Human Genome Project to clinically relevant material and data depends on ventures such as those involving Ardais and academic centers. The bioethical questions and repercussions of these partnerships, however, continue to be problematic.

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Purple spots and chickenpox

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QUESTION: The mother of a 9-year-old girl calls the nurse to ask if she should bring her daughter to the clinic because her daughter now has purple spots on her body after a chickenpox infection. The mother noted the onset of the purple spots the day before and denies any history of trauma. The chickenpox had begun 10 days ago and was mostly healing. She was told to bring in the patient immediately for evaluation.

The young girl appeared fatigued. She was holding a wad of tissues in her mouth to stop the bleeding from a baby tooth that had fallen out 2 days ago. Most of the purple spots were seen on the legs (figure). Blood pressure, pulse, and temperature were normal. The examination showed no other bleeding sites than the tooth socket, which was oozing slowly. The old varicella lesions were in various stages of reepithelialization.

What are the purple spots, and what is the pathogenesis? How would you diagnose this condition, and what is the appropriate treatment?

Purple spots appeared in the aftermath of chickenpox

ANSWER: The purple spots are purpura and petechiae. The most likely cause is a low platelet count in the condition of varicella-associated thrombocytopenia. The continued bleeding from the tooth socket supports the hypothesis of a bleeding disorder. A platelet count with a complete blood count, prothrombin time, and partial thromboplastin time were obtained immediately. The platelet count was 12×10^9/L (12,000/μL). This severe thrombocytopenia explains the purpura, petechiae, and oral bleeding. The presumptive diagnosis was virus-associated idiopathic thrombocytopenic purpura or, more specifically, a varicella-associated thrombocytopenia. Although this is a rare condition, it has been reported numerous times in the world's medical literature.

PATHOPHYSIOLOGIC MECHANISM

Rand and Wright state : "Two-thirds of children with acute idiopathic thrombocytopenic purpura (ITP) have a history of an infectious illness a few days to a few weeks before the onset of thrombocytopenia."[1] In some of these children, a specific virus can be identified, such as varicella zoster virus, rubella, Epstein-Barr virus, influenza virus, and human immunodeficiency virus. Research suggests that there is a molecular mimicry between the viral antigens and platelet surface glycoproteins so that host antibodies cross-react with the platelets' membrane antigens and increase the clearance of platelets.[2] This autoimmune phenomenon occurs during the viremic phase of the acute viral infection and leads to thrombocytopenia.

TREATMENT

The major treatments reported for virus-associated ITP include intravenous immune globulin and high-dose parenteral steroids. Although these treatments have been used successfully, no randomized controlled trials have been done to compare these treatments with each other or with placebo.

PATIENT'S COURSE

The patient was admitted to the hospital where she received intravenous immune globulin and intravenous methylprednisolone. The following day, her platelet count was up to 50×10^9/L. The next day, her platelet count was more than 100×10^9/L. The bleeding from her tooth socket stopped completely, and no new purpuric lesions developed. The following day, her platelet count was completely normal, and she was discharged home with follow-up to monitor her platelet counts. The patient did well, and the acute ITP resolved completely.

PREVENTION

This complication of varicella can be prevented with the varicella vaccine. Before the availability of varicella vaccine, varicella disease was responsible for 11,000 hospitalizations and 100 deaths each year in the United States.[3] Even though many of the deaths and hospital admissions were due to varicella pneumonia, varicella-associated thrombocytopenic purpura is a potentially preventable complication. This case underscores the need to adequately immunize our population with the varicella vaccine.

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Mail

Intractable or chronic pain: there is a difference

To the editor,

Chronic pain is usually defined as any persistent or intermittent pain that lasts more than 3 months.[1] When this definition is used, more than 40% of the general population reports having chronic pain, primarily due to arthritis or other musculoskeletal disorder.[2] Based on our clinical observations, within the chronic pain population, a subgroup has an intractable pain syndrome or disease. All have incurable, extremely painful conditions, as evidenced by failure of various interventions to control their pain, including surgery, nerve blocks, physical rehabilitation, and weak opioids. Patients describe their pain as constant, debilitating, and potent enough to interfere with sleep and sexual function. Many report suicidal thoughts for the sole purpose of stopping the pain, incessant crying spells, fatigue, depression, social isolation, restriction of mobility, and numerous bed- or couch-bound days.

California, Oregon, and Washington have passed "intractable pain" laws, primarily to allow physicians to legally prescribe opioids to needy pain patients

Objective assessment of these patients invariably reveals intermittently elevated blood pressure and pulse rate and abnormal concentrations of serum cortisol and other adrenal hormones, indicating the presence of a severe and extended stress state.[3] Others have also recently postulated that severe chronic pain may produce an extended, destructive stress state characterized by neuroendocrine dysregulation, fatigue, dysphoria, myalgia, and impaired mental and physical performance.[4]

We suggest that this constellation of abnormalities be called "intractable pain disease." About a dozen states, including California, Oregon, and Washington, have passed "intractable pain" laws, primarily to allow physicians to legally prescribe opioids to needy pain patients. Although the legal and legislative definition of "intractable" in the various state laws may be vague, the legislative intent of all these laws is clearly to identify the subgroup of patients with chronic pain who require opioids. It, therefore, appears prudent and practical to adopt the term intractable for those patients with severe, chronic pain who demonstrate the extended, severe stress response described above. Although some other name could be adopted for this tragic group of afflicted patients, an intractable pain syndrome clearly needs to be recognized, treated, and researched independently as a separate disease that differs from simple chronic pain whose symptoms may merely be minor, mild, intermittent, or persistent for longer than 3 months.

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Competing interests: None declared

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Original Research

US women's attitudes to false-positive mammography results and detection of ductal carcinoma in situ: cross-sectional survey

ABSTRACT **Objective** To determine women's attitudes and knowledge of both false-positive mammography results and the detection of ductal carcinoma in situ after screening mammography. **Design** Cross-sectional survey. **Setting** United States. **Participants** A total of 479 women aged 18 to 97 years who did not report a history of breast cancer. **Main outcome measures** Attitudes and knowledge about false-positive results and the detection of ductal carcinoma in situ after screening mammography. **Results** Women were aware that false-positive results do occur. Their median estimate of the false-positive rate for 10 years of annual screening was 20% (25th percentile estimate, 10%; 75th percentile estimate, 45%). The women were highly tolerant of false-positive results: 63% thought that 500 or more false-positives per life saved was reasonable, and 37% would tolerate a rate of 10,000 or more. Women who had had a false-positive result (n = 76) expressed the same high tolerance: 30 (39%) would tolerate 10,000 or more false-positives. In all, 62% of women did not want to take false-positive results into account when deciding about screening. Only 8% of women thought that mammography could harm a woman without breast cancer, and 94% doubted the possibility of nonprogressive breast cancers. Few had heard of ductal carcinoma in situ, a cancer that may not progress, but when informed, 60% of women wanted to take into account the possibility of it being detected when deciding about screening. **Conclusions** Women are aware of false-positive results and seem to view them as an acceptable consequence of screening mammography. In contrast, most women are unaware that screening can detect cancers that may never progress but think that such information would be relevant. Education should perhaps focus less on false-positive results and more on the less-familiar outcome of the detection of ductal carcinoma in situ.

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INTRODUCTION

Screening mammography is vigorously promoted in the United States. With the exception of the US Preventive Health Services Task Force, most professional organizations recommend that women begin annual or biannual screening at 40 years of age.[1-3] Mammography is promulgated by hospitals, insurance plans, and breast care centers. Efforts for quality improvement commonly focus on increasing the screening rates for breast cancer, and health plans highlight these rates on cards used for reporting quality of health care. Although the possible benefits of mammography have been much discussed, the possible harms have not.

The harm that has received the most attention is false-positive results. Mammograms that give false-positive results are common. A 60-year-old woman screened annually for 10 years has about a 50% chance of having at least 1 false-positive that leads to follow-up testing and about a 20% chance of a false-positive that leads to biopsy.[4] Consequently, many people are concerned about the physical, psychological, and economic costs of false-positive results.[4-10] Several experts in screening have concluded that women would benefit from education about false-positive results if they are to make informed decisions about whether to undergo, or to continue with, screening.[2,11-13]

Little attention has been paid to the increasingly more frequent detection of ductal carcinoma in situ, a subtle but possible harm of screening.[14] Although the clinical course of ductal carcinoma in situ is poorly understood, most lesions do not progress.[14-17] Consequently, more women with lesions that would never have become clinically apparent are worried about cancer, and most will undergo invasive treatment of unknown benefit (for example, mastectomy or lumpectomy with radiation).[14]

Whether or how women offered screening are being counseled about false-positive results and ductal carcinoma in situ is not known. To determine what women know, we conducted a national survey of US women, a population with high exposure to mammography—more than 85% of US women aged 40 years or older have had at least 1 screening mammogram.[18] We wanted to find out if women are aware of false-positive results and if they have a sense of the chance of having 1, if false-positive results are tolerated because women have an unrealistic sense of the benefit of mammography, and if women are aware of ductal carcinoma in situ and, if not, whether they want to know about it.

PARTICIPANTS AND METHODS

Design

We randomly selected women from details compiled from telephone directories and administrative records (for example, applications for a driver's license, electoral registries, and house purchases) by National Decision Systems,

Summary points

What is already known on this topic

- False-positive results and diagnoses of nonprogressive cancer are recognized problems of screening mammography
- Little is known about how women feel about these problems

What this study adds

- Almost all (99%) of 479 women knew that false-positive mammograms occur
- Women do not seem to think false-positive mammograms are an important harm of screening—even women who have had a false-positive result
- Women's tolerance for false-positives is not explained by overly optimistic beliefs about the benefit of mammography
- Few (6%) of the women were aware of the possibility of nonprogressive cancer

Atlanta, GA. We restricted our sample to the 80% of US women in households with telephones. We used stratified random sampling to oversample women of screening age. Specifically, we selected women by age (18-39 years old, 200 women; 40-49, 250; 50-69, 250; and 70 or older, 100), estimated income (income more or less than twice the 1992 poverty threshold for a family of 4 people[19]), and area of residence.

From August to October 1997, we mailed a questionnaire (with $2 as an incentive) to 800 women. We chose to conduct a postal survey to use visual analogue scales. We mailed reminder letters to nonrespondents after 2 weeks, sent a second copy of the questionnaire after 4 weeks, and attempted to telephone those who had still not responded after 6 weeks.

Of the 800 people selected, 33 were ineligible (21 had died, and 12 were men) leaving 767 possible respondents. Of these women, 55 had incorrect addresses, 2 did not speak English, and 207 did not return the questionnaire. Overall, 503 of the 767 women (65.6%) returned completed questionnaires. We report on the 479 respondents with no history of breast cancer.

Survey

We developed a 13-page questionnaire as part of a larger project on women's decision making about mammography. A pilot was tested on women veterans served by the Veterans Affairs Medical Center at White River Junction, Vermont.

Visual analogue scales

We asked women to estimate the sensitivity and false-positive rate of mammography with a previously validated visual analogue scale.[20] To familiarize respondents with the scale, we included 2 practice questions about events having extreme probabilities. Overall, 94% of respondents used the correct end of the scale for each event—close to 1 for the chance of stopping at a red light, and close to 0 for the chance of being hit by a meteorite.

We also asked women to compare the benefits of mammography with other preventive activities that might extend the life of a 60-year-old woman (figure 1). For each prevention strategy, we asked respondents to mark anywhere on a line scaled from "much less benefit" to "much greater benefit" compared with 10 years of annual mammography, the midpoint being "same benefit." We measured the distance of each woman's mark from "much less benefit" and calculated the median value.

Analysis

Because we used stratified random sampling, we calculated sample weights to account for the probability of selection and to compensate for small differences in response rates across sample strata. We then adjusted the sample distribution to conform to known marginal distributions of the US population, based on data from the 1990 US census,[19,21] by creating "balance weights."[22] Because the crude results and the weighted results yielded almost identical results, for simplicity we present the crude data. Based on our sample size, we estimate the margin of error of the results to be 4% to 6% in either direction.[23] All analyses were done with commercially available software (STATA; Stata Corporation, College Station, TX).

RESULTS

Sample characteristics

Table 1 shows the characteristics of the women. Respondents were from all 50 states and the District of Columbia. Most women reported having had at least 1 mammogram: 35% of women younger than 40 years, 87% of women in their 40s, 93% of women aged 50 to 69 years, and 87% of women aged 70 or older.[3] Similarly high proportions of women planned to have a mammogram in the next 2 years.

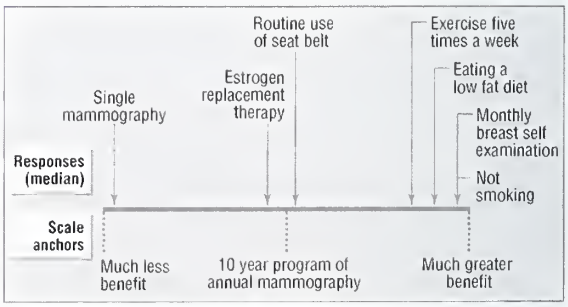

Figure 1 Women's ranking of benefits of health-promoting activities and 10-year program of mammography for extending life in a 60-year-old woman. Arrows show median response for each strategy.

Table 1 *Characteristics of sample compared with women 18 years and older from 1990 US census**

Characteristics	Patients (n = 479)	1990 US census, %
Age, yr		
18-39	120 (25)	46
40-49	153 (32)	16
50-69	158 (33)	24
≥70	48 (10)	14
Ethnicity		
White	431 (90)	78
African American	19 (4)	11
Hispanic	10 (2)	7
Other	19 (4)	4
Household income, $		
<10,000	24 (5)	13
10,000-24,999	86 (18)	24
25,000-49,999	158 (33)	33
50,000-99,999	163 (34)	22
≥100,000	48 (10)	8
Highest level of education		
<High school graduate	29 (6)	25
High school degree	268 (56)	53
College degree	139 (29)	17
Postgraduate degree	43 (9)	5
Region		
Northeast	67 (14)	21
Midwest	115 (24)	24
South	153 (32)	35
West	144 (30)	20

*Values are numbers (percentages) unless stated otherwise. 95% confidence intervals ranged from 4% to 6% in either direction for all percentages.

Perception of harm

Overall, 441 (92.1%) women believed that mammography could not harm a woman without breast cancer (table 2). Of the 38 women who thought harm was possible, 30 responded to our request for an explanation. The most common responses were exposure to radiation (16 women), stress or anxiety (4 women), and false-positive results (3 women). None mentioned the effects of treating nonprogressive cancer.

False-positive results

Overall, 99% of women believed that false-positive results (ie, abnormal mammogram that leads to a breast biopsy that turns out negative for cancer) occur during a 10-year program of annual mammography beginning at age 60 years. The women's median estimated chance of a false-positive result during such a program was 20%. This estimate is in line with a recent report citing a 10-year 47% probability of a false-positive mammographic result leading to any follow-up testing for a 60-year-old woman and a 19% probability of a false-positive mammographic result leading to a biopsy.[4]

To understand the importance of false-positive results, we asked respondents whether they wanted to take into account such results when deciding about mammography; only 38% did. When asked how many false-positives would be acceptable for each life saved, women showed a high tolerance: 63% would tolerate 500 or more false-positives, and 37% would tolerate 10,000 or more (figure 2). The best estimate of the actual number of false-positive mammograms for each life saved is somewhere between 30 and 200, assuming 2 to 6 lives saved for every 1,000 women screened for 12 years[24,25] and a 10-year false-positive rate between 20% and 40%.[4] Thus, the actual number of false-positives is far below the number most women deemed acceptable.

Women who had had a false-positive mammogram expressed a similarly high tolerance for false-positive results. Seventy-six women (16%) reported having had a false-positive mammogram—that is, a breast biopsy but no diagnosis of breast cancer. In this subgroup, 71 (93%) believed that mammography could not harm a woman who turned out not to have breast cancer, 27 (36%) wanted to take false-positives into account when deciding on screening, 54 (71%) would tolerate 500 or more false-positives per life saved, and 30 (39%) would tolerate 10,000 or more (figure 2).

Perception of benefit

To explore whether this high tolerance reflected an unrealistic sense of the benefit of mammography, we examined perceptions of benefit. As expected, most women (94%) thought that women whose breast cancer was diagnosed by screening mammography benefited from having been screened (table 2). Although most believed that mammography reduced the chance of dying of breast cancer, none thought it reduced the risk to 0. The most common expectation was that mammography would reduce the chance of dying of breast cancer by half, and the second most common expectation was that it would reduce the chance by a third[24,25] (we considered this to be the correct answer, but a recent study suggests that a one-third reduction in risk may be an overestimate[26]). Women were aware that mammography did not find all cancers. Their median estimated sensitivity for a single mammogram (for a 60-year-old woman) of 73% underestimated the reported sensitivity of 94% (95% confidence interval, 83%-99%).[27]

Most women (82%) recognized that a 10-year program of mammography was more beneficial than single mammography (figure 1). Women rated health-promoting strategies like not smoking, exercising regularly, and eating a low-fat diet as much more beneficial than mammography. Surprisingly, women believed breast self-examinations to be more beneficial than the 10-year program of annual mammography.

Table 2 *Women's perceptions of benefits and harms of screening**

Perception	No. (%) of patients
Perception of harms	
Do you agree that "if a woman getting mammograms turns out not to have breast cancer, she may have been harmed by the mammograms"?	38 (8)
False-positives	
"Imagine a typical, healthy 60-year-old woman. Assume that you know nothing else about her. Suppose that this 60-year-old woman has yearly mammograms for the next 10 years and she does not have breast cancer. What is the chance that she will have a 'false alarm' where 1 of her mammograms will look like she has cancer even though she doesn't?	Median 20/100, 25th percentile = 10%, 75th percentile = 48%
"Is information about false alarms something you want to factor into your decision about getting a mammogram"?†	182 (38)
Nonprogressive cancer	
Do you agree that "some types of breast cancer grow so slowly that even without treatment they would not affect a woman's health"?	34 (7)
Presentation of ductal carcinoma in situ (DCIS) information‡: "Have you heard about DCIS before this survey?"	29 (6)
"Is information about DCIS something you want to factor into your decision about getting a mammogram?"†	287 (60)
Perception of benefits	
Do you agree that "if a woman getting mammograms turns out to have breast cancer, she may have benefited from the mammograms"?	450 (94)
Sensitivity of mammography	
"Imagine a typical, healthy 60-year-old woman. Assume that you know nothing else about her. Now imagine that this 60-year-old woman has breast cancer but no obvious symptoms. What is the chance a mammogram will find the cancer?"	Median 73/100, 25th percentile = 50%, 75th percentile = 86%
Magnitude of benefit	
"All things being equal, if this 60-year-old woman got yearly mammograms for the next 10 years, she would have . . ."§	
A higher or unchanged chance of dying of breast cancer	34 (7)
A lower chance of dying of breast cancer	
By one fifth to one tenth	62 (13)
By one third	120 (25)
By a half	263 (55)
Reduced to zero	0 (0)

*95% confidence intervals ranged from 4% to 6% in either direction for all percentages. Questions preceded by "do you agree that" used a 5-point Likert scale (strongly agree to strongly disagree); the proportion agreeing are those who answered "strongly agree" or "agree."
†Percentage of women answering "yes."
‡Women were given a brief explanation of ductal carcinoma in situ as a lesion that does not always progress to invasive cancer.
§Actual response choices were: lower by one half, lower by one third, lower by one fifth to one tenth, no change, higher by one fifth to one tenth, higher by one third, higher by one half.

Nonprogressive cancer

Few women knew about the possibility of nonprogressive breast cancer (table 2). Only 7% agreed that some breast cancers grow so slowly that even without treatment they would not affect a woman's health. We gave the following brief explanation of ductal carcinoma in situ:

> We would like to ask your opinion about ductal carcinoma in situ, or DCIS, a breast abnormality that can only be picked up by mammograms. Cancer specialists are confused about DCIS because sometimes it becomes invasive and sometimes it doesn't. If DCIS does not become invasive, it will not affect how long a person will live even without treatment. Doctors don't know which DCIS will become invasive. Nowadays, almost everyone with DCIS gets treated. Many people receive surgery, chemotherapy, or irradiation who would never have gotten sick. For these people, treatment provides no physical benefit.

Only 6% of women reported having heard of ductal carcinoma in situ by name or corresponding to the description provided, and 60% wanted to take ductal carci-

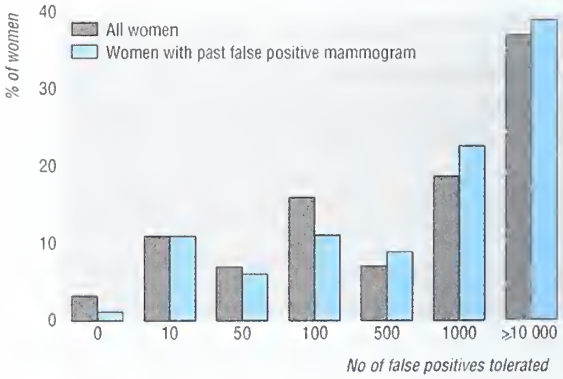

Figure 2 Number of false-positive results women were prepared to tolerate for each life saved

noma in situ into account when deciding about mammography, with interest highest among younger women (71% of women aged 18-39 years).

To assess how information about nonprogressive cancer might influence decision making, we asked women to decide about treatment of ductal carcinoma in situ under different assumptions of its probability of becoming invasive (figure 3). In the hypothetic scenario, more women chose treatment as the chance of invasion increased. At a 1% chance of ductal carcinoma in situ becoming invasive, 42% of women chose treatment whereas at a 33% chance of invasion, 78% chose treatment. The limited published estimates of the chance of ductal carcinoma in situ becoming invasive vary and are as high as 33%.[14,17]

DISCUSSION

The women in our study were aware of false-positive results from screening mammography but seemed to view them as an acceptable consequence of screening. Although studies attest to the short-term physical and psychological effects of false-positive results,[5-9] our respondents were highly accepting of them: most would not take them into account when deciding about screening, and almost 40% would tolerate 10,000 or more false-positives requiring biopsy for each life saved.

One explanation for this high tolerance is that women have an overly optimistic sense of the benefit of mammography. We found no evidence to support this explanation. No respondent thought screening mammography eliminated the chance of dying of breast cancer. Women were aware that mammography misses some cancers (actually underestimating the reported sensitivity). Most women also recognized that health-promoting behaviors like not smoking, exercising regularly, and eating a low-fat diet were more beneficial than mammography in prolonging life, which is true for the average 60-year-old woman.[28]

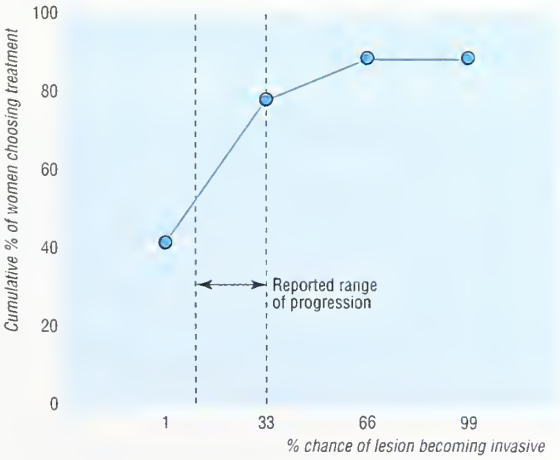

Figure 3 Women's threshold for treatment of ductal carcinoma in situ according to its chance of becoming invasive

John Pineda/AP

Mammography is vigorously promoted in the United States

Alternatively, it might be posited that women did not fully understand the consequences of a false-positive result (for example, anxiety, pain, inconvenience, or extremely rare harms such as severe infection or death related to anesthesia). We found, however, that women who had had false-positive mammograms expressed the same high tolerance as women who had not. Thus, women seemed to believe that false-positive results are worth the reassurance of being told they do not have cancer. Similarly, Gram and colleagues found that almost half of women with false-positive mammograms viewed the experience as having an overall positive effect on their lives,[8] and most women continue to undergo mammography.[29]

Women's perceptions about a possible diagnosis of ductal carcinoma in situ differed noticeably from their perceptions about false-positive mammograms. In contrast to false-positives, most women were unaware of nonprogressive forms of breast cancer and even doubted their existence. Once informed about nonprogressive cancer, the women seem concerned. Most wanted to take into account the possibility of ductal carcinoma in situ when deciding about screening. Younger women, for whom 90% of the cancers found by screening mammography are ductal carcinoma in situ,[15] were the most interested in such information. In addition, women's reported willingness to treat ductal carcinoma in situ increased as we hypothetically increased the chance of ductal carcinoma in situ progressing to invasive breast cancer, suggesting that such information might influence decisions.

Limitations

One limitation of our study is the representativeness of the sample: we did not include women in households without a telephone and those who requested that their name be removed from the database. This left about 80% of US women eligible for sampling. Second, although our sample represents women across a broad range of age, education, and income, it differed from the general popu-

lation: the women who responded were wealthier, better educated, and almost all were white. Minority women and women with the lowest socioeconomic indicators were underrepresented. Subsequent studies are needed to assess whether such women have different perceptions.

One concern is the possibility of systematic bias in our sample because respondents differed from nonrespondents. Our response rate of 66% lessens but does not eliminate this concern. Respondents and nonrespondents did not differ by age (the 1 variable available for comparison). Our main findings were extreme enough (for example, only 7% of women were aware of nonprogressive breast cancer), however, that even if respondents and nonrespondents differed noticeably, our overall conclusions should remain robust. Although the survey was long and complex, response rates for items were high. Response rates were lowest for the question on the treatment threshold for ductal carcinoma in situ (82%) and averaged 98% for all other questions.

Although experts on screening have focused much attention on the anxiety experienced by women with false-positive mammograms,[13] clinicians counseling women about mammography should spend less time reviewing what most women know and accept—that is, that false-positives are part of screening. In contrast, more time should probably be spent educating women about the less familiar outcome of the ambiguity associated with the detection of ductal carcinoma in situ.

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Contributors L M S and S W collaborate on all work and are the joint principal investigators on the Department of Defense grant "enhancing informed decision making about mammography"; they will act as guarantors for the article. They initiated and coordinated the formulation of the study hypotheses, discussed core ideas, designed the study protocol, developed the survey, and participated in the data collection, analysis, and writing of the paper. H C S and B F participated in formulating the study hypotheses, discussing core ideas, designing the study, developing the survey, and writing the paper. H G W participated in the formulation of study hypotheses, discussing core ideas, designing the study, developing the survey, the analysis, and writing of the paper.

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COMMENTARY

Women should be fully informed of the potential benefits and harms before screening mammography

Based on their survey of women's attitudes about screening mammography, Schwartz and colleagues conclude that women are knowledgeable of the chance of a false-positive result and accept this risk as a consequence of undergoing screening mammography. It is not clear, however, whether the authors accurately assessed women's true tolerance of false-positive mammography results because their survey did not describe the spectrum of physical and psychological sequelae of a false-positive result (for example, additional diagnostic evaluations and associated morbidity and anxiety).[1-3] Thus, the proportion of women who are tolerant of false-positive mammography results may have been overestimated because the possible harms of screening mammography were not fully described. Even so, 38% of women surveyed indicated that they would want to factor information about the consequences of false-positive results into their decision about undergoing screening mammography. If nearly 2 of every 5 women desire such information, then they should be informed of the possible harms, as well as the benefits, of screening mammography.

The authors attempt to bolster their conclusion by reporting that women who had both a positive mammography result and subsequent benign findings on tissue biopsy expressed the same high tolerance for false-positive results as all of the women surveyed. However, women who have positive mammography results that subsequently lead to biopsy account for only 25% of women with false-positive results.[4] Thus, these women's tolerance of false-positive results may not accurately reflect the views of all women who have false-positive results. Women who undergo breast biopsy for positive results are often so relieved when they find out that they do not have breast cancer that they might understandably—but somewhat ironically—have a high tolerance of false-positive results.

The authors found that a significant proportion (55%) of women overestimate the benefit of mammography, and that only 25% accurately reported that the chance of dying of breast cancer would be reduced by 30% for a 60-year-old woman undergoing screening mammography. Nonetheless, Schwartz and associates conclude that the high tolerance for false-positive results is not explained by overly optimistic beliefs of the benefits of mammography. One interpretation of the results is that women do overestimate the benefit of screening and that such misperceptions may explain why some women did not want to factor information about the consequences of false-positives into their decision about screening mammography.

The authors found that few women (6%) were knowledgeable about ductal carcinoma in situ (DCIS). When women were informed about DCIS, 3 of every 5 women wanted to take into account the chance of it being detected when deciding whether to undergo screening mammography. This is an important finding and suggests that information about DCIS should be included in educational materials and discussions about the possible benefits and harms of screening mammography. We were involved in designing and writing a Web site (http://mammography.ucsf.edu/inform/index.cfm) that gives an example of how DCIS may be explained to women. The site states that

> DCIS lesions contain cells that appear to be cancer but not all such lesions behave as cancer, ie, they will not spread outside the ducts and invade surrounding tissue nor will they be life threatening. In other words, only some DCIS will eventually become invasive cancer. What percentage will become invasive cancer is not known. Almost all women who have DCIS detected are treated by surgery, either a mastectomy (removal of the breast) or by lumpectomy (excision of the lesion) with or without radiation.

Additional information that could be conveyed to women is the absolute benefit of detecting DCIS. For example, for every 10,000 women aged 70 years and older screened for 10 years, 65 cases of DCIS will be detected and surgically treated with mastectomy or lumpectomy and only 1 death from invasive breast cancer averted.[5]

To encompass a range of individual preferences, women should be provided with estimates—in absolute terms—of the possible benefits and harms of mammography to make an informed decision about screening (see box). Women who easily tolerate the additional tests that

Estimates that should be provided to a woman for informed decision making before mammography

- Individual risk of invasive breast cancer and DCIS
- Age-specific chance of an abnormal result
- Age-specific chance of a false-positive result
- Chance that mammography may miss cancer
- Expected absolute reduction in risk of breast cancer deaths among women in her age group who undergo screening mammography compared with women who do not

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Potential Benefits & Risks of Mammograms

About this Web Site: Breast cancer is a commonly diagnosed cancer in women. Mammograms are one way to detect breast cancer. This Website provides up to date information about the potential benefits and risks of screening mammograms according to a woman's age. Prior to placing this Web site on the Internet, its content was reviewed by medical researchers and by breast cancer advocates for completeness, clarity and bias. The Deputy Director, Division of Cancer Prevention and Control at the National Cancer Institute and the Associate Director for Science, Division of Cancer Prevention and Control at the Centers for Disease Control reviewed and approved the content of the program for linkage to their Internet sites.

This Web site, at http://mammography.ucsf.edu/inform/index.cfm, gives clinical information about ductal carcinoma in situ (DCIS)

are recommended following an abnormal screening result and want to do everything possible to decrease the chance of death from breast cancer, even if certain harms are involved, will likely choose to undergo screening mammography. On the other hand, women who feel that the small incremental risk of breast cancer death associated with not being screened is outweighed by the fairly high likelihood of a false-positive result, the additional testing, and the anxiety may rationally choose not to have screening mammography.

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5-Year analysis of mushroom exposures in California

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ABSTRACT **Objective** To evaluate outcomes following toxic mushroom ingestions. **Design** Retrospective data analysis. **Methods** We analyzed American Association of Poison Control Center data for California from 1993 through 1997. **Results** A total of 6,317 exposures occurred during the study period. Most (n = 6,299 [99.7%]) were acute exposures, and the rest (0.3%) were chronic; 87.6% (n = 5,536) were unintentional. Most (n = 4,235 [67.0%]) were in children younger than 6 years, and of these, only 6.0% experienced any clinical effects. The most common symptoms in patients aged 6 years and older were vomiting in 588 patients (28.2%), nausea in 307 patients (14.7%), diarrhea in 263 patients (12.6%), and abdominal pain in 221 patients (10.6%). No effects were seen in 3,131 (49.6% of all patients). Major effects were seen in only 17 patients (0.3%). Only 61 patients (1.0%) were admitted to a critical care unit. Death occurred in a 32-year-old adult who ate foraged mushrooms. Of all patients, 1,375 (21.8%) received no therapy or were observed only. **Conclusions** Most mushroom exposures were acute and unintentional and occurred in children younger than 6 years. Major toxic reactions or death was uncommon.

INTRODUCTION

Foraging for wild mushrooms is popular in the United States. California has a large number of species of mushrooms, including toxic species. One of the limitations in assessing possible wild mushroom poisoning is the lack of outcome data following ingestions. We performed this study to evaluate outcomes following foraged mushroom ingestions.

METHODS

The American Association of Poison Control Centers (AAPCC) comprehensive poisoning surveillance database, Toxic Exposure Surveillance System (TESS), was retrospectively analyzed for the years 1993 through 1997 for the entire state of California. These data were collected by poison control centers in the state by telephone hotlines. Reports to poison centers included in TESS originate from the public and from health care professionals and include both patients managed at home or at the site of the exposure and those managed in hospitals, emergency departments, or other health care facilities. The TESS data for each case of poisoning include the substances implicated (mushroom), patient age, outcome, clinical effects, exposure route, whether acute or chronic ingestion, and the level of health care intervention used.[1]

The following fields were extracted from the data set: patient age, management site, decontamination therapy, related symptoms, site of exposure, and patient outcomes. The outcome definitions were those used by the AAPCC[2]:

- no effect: no symptoms developed as a result of the exposure;
- minor effect: the patient exhibited some symptoms as a result of the exposure, but they were minimally bothersome;
- moderate effect: the patient exhibited symptoms that were more pronounced, more prolonged, or more systemic as a result of the exposure, and the symptoms were not life-threatening, but usually some treatment was indicated;
- major effect: the patient exhibited some symptoms as a result of the exposure, which were either life-threatening or resulted in substantial toxic effects; and
- death: the cause of death was determined to be probably or undoubtedly related to the exposure.

All results are reported as descriptive statistics.

RESULTS

A total of 6,317 exposures were reported to California poison control centers during the 5-year study period. Most (99.7%) of the exposures (n = 6,299) were single, acute poisonings, and the rest (n = 16 [0.3%]) resulted from long-term ingestions. In all, 87.6% of all exposures (n = 5,536) were unintentional. In 4,235 of the incidents of exposure, the patients were younger than 6 years; 541 occurred in 6- to 12-year-olds, 667 occurred in 13- to 19-year-olds, and 865 occurred in patients 20 years of age or older. The age was unrecorded in 9 reports.

The most common geographic site of exposure (n = 5,798 [91.8%]) was a residence, followed by a school (n = 223 [3.5%]). The mushroom was the single substance involved in 6,201 exposures (98.2%). The species of mushroom ingested was identified in only 334 cases (5.3%), and in these, it was usually (n = 254) a psilocybin-containing variety. Most psilocybin ("magic mushroom") ingestions (n = 251 [98.8%]) were intentional and occurred mainly in adolescents and young adults (mean [±SD] age, 18.9 [±6.4] years; median age, 18 years; and range, 1-42 years). The number of psilocybin ingestions has increased annually, from 16 in 1993 to 29 in 1994, 43 in 1995, 69 in 1996, and 97 in 1997.

Of the 4,235 exposed children younger than 6 years, 3,980 (94.0%) experienced no effect following the exposure, minor effects were seen in 216 (5.1%), moderate in 34 (0.8%), and major in 1 (0.02%). The most common symptoms in patients aged 6 years and older were vomiting in 588 (28.2%), nausea in 307 (14.7%), diarrhea in 263 (12.6%), abdominal pain in 221 (10.6%), and hallucinations in 149 (7.2%). No death occurred in patients younger than 20 years. Elevated hepatic aminotransferase levels, defined as serum aspartate aminotransferase (previously SGOT) or serum alanine aminotransferase (previously SGPT) levels of greater than 100 U/L, were seen in 32 patients (0.5%), of whom only 4 were younger than 6 years. Only 1 of these children had serum hepatic aminotransferase levels greater than 1,000 U/L.

A total of 3,657 patients (57.9%) were treated on site, whereas 1,808 (28.6%) were treated and released from a health care facility. Of children younger than 6 years, 2,957 (69.8%) were treated at a non–health care facility (home or other residence). An additional 974 (23.0%) were treated and released from a health care facility (such as an emergency department, urgent care facility, or physician's office). Only 31 children younger than 6 years (0.7%) were admitted to a hospital.

The following data give the clinical outcome of all exposures studied: no effect (n = 3,131 [49.6%]), minor (n = 636 [10.1%]), moderate (n = 264 [4.2%]), major (n = 17 [0.3%]), and 1 death (0.02%). Follow-up to a "known" outcome (according to TESS criteria) was not performed in 2,058 cases (32.6%). However, in most cases of exposure (n = 1,044 [16.5%]), follow-up to a known outcome was not performed because the exposures were thought to be either "nontoxic" (n = 341 [5.4%]) or "minimally toxic" (n = 703 [11.1%])—that is, resulting in mild, self-limiting symptoms. In 1,014 cases (16.1%), the exposure was thought to be potentially toxic but could not be followed up because of insufficient patient data (for example, either no phone number or an incorrect phone number given).

Only 61 (1.0%) patients were admitted to a critical care unit, and 94 (1.5%) were admitted to a non–critical

Amanita muscaria, the most recognizable of the *Amanita* family

care unit. Only 1 death was reported during the study period, and this occurred in a 32-year-old adult who ate foraged mushrooms. A total of 1,375 patients (21.8%) received no therapy or observation only. Of those who were treated, 2,215 (35.1%) received ipecac syrup, 975 (15.4%) received a single dose of activated charcoal, 77 (1.2%) underwent gastric lavage, and 41 (0.6%) received multiple doses of activated charcoal.

DISCUSSION

The exact identification of mushroom species can be difficult.[3] Substantial morphologic variations can occur in the same mushroom species depending on the season, geographic location, and maturity of the fungus. Fortunately, most mushrooms ingested are either nontoxic or gastrointestinal irritants, resulting in mild to moderate toxic effects.[3] Toxic species of mushrooms can be divided into 8 broad categories: cyclopeptides, orellanine, monomethyl hydrazine, *Coprinus* species, ibotenic acid, muscarinic, *Psilocybe*, and gastrointestinal irritants.[4,5] Of these, cyclopeptide or amatoxin-containing species represent the greatest danger. Members of this group include *Amanita* and *Gallerina* species and have the common names of "death cap" (*Amanita phalloides*) or "destroying angel" (*Amanita ocreata*).[6,7]

The clinical presentation following a cyclopeptide mushroom ingestion can include severe centrilobular hepatic necrosis clinically indistinguishable from acetaminophen poisoning. Although rare, this type of toxic reaction accounts for 95% of mushroom-related deaths in North America.[5] The only death reported in our series resulted from the ingestion of foraged cyclopeptide mushrooms.

Because of the inability of accurate mushroom identification, the onset of clinical symptoms has been suggested as a good biomarker for the likelihood of the ingestion of an amatoxin-containing species.[4] Amanita mushrooms generally manifest gastrointestinal symptoms, but effects are delayed for more than 6 hours following ingestion. Persons who ingest typical gastrointestinal irritant mushrooms such as *Chlorophyllum* species generally have symptoms within 30 minutes to a few hours following ingestion.[4,5] One caveat to this rule of thumb is that the ingestion of foraged mushrooms often includes several species, thereby giving a misleading clinical course if gastrointestinal symptoms are seen within the first few hours of ingestion. The 6-hour rule may be more helpful when a child accidentally ingests a single species of mushroom.

Because of the inability to identify mushrooms and the lack of an effective antidote for amatoxin-containing species, much attention has been focused on gastrointestinal decontamination in cases of exposure to these species. The use of ipecac syrup, once a mainstay of poisoning treatment of mushroom ingestions, has been questioned.[8] Specifically, problems with ipecac include its inability to effectively empty the stomach, its contraindications of decreased mental status and risk of seizures, and most important, the loss of the gastrointestinal monitoring variable, particularly in children ingesting a single species of mushroom. More recently, attention has been focused on home and prehospital administration of activated charcoal in these cases. Prehospital administration of activated charcoal appears to be a promising decontamination technique, but its efficacy is dependent on the dose administered, patient acceptability, and availability for home use.[9]

Our results demonstrated that most mushroom exposures in California from 1993 through 1997 were acute, unintentional exposures in children younger than 6. No effects were seen in 94% of these children, suggesting that major toxic reactions or death may be uncommon following acute, nonintentional mushroom ingestions in these patients. Consistent with previous reports, the only death seen in this study occurred in an adult who ate foraged mushrooms with a meal. Possibly, young children would rarely, if ever, ingest enough amanita mushrooms to lead to hepatic damage. This is consistent with the lack of such cases in poison center records and the recent medical literature. However, it is still prudent to consider the possibility of hepatotoxic mushroom ingestion in children who present with delayed symptoms after eating mushrooms or where identification is not possible.

Our study is one of the first to evaluate a possible difference between toxic reactions encountered with foraged mushrooms as opposed to accidental pediatric exposure. Although our numbers are large compared with

other toxin and drug poisonings reported to California poison control centers, morbidity and mortality are rare with most of these cases. How many years of exposures would be required to generate enough experience to generalize our findings into management recommendations is difficult to estimate because comfort levels with treatment of these cases would likely vary among health care providers. It may be of benefit to health care providers to develop a sense of the rarity of the occurrence of major toxic reactions and death in most unintentional childhood mushroom ingestions.

Our study is also limited by the number of cases unavailable for follow-up and the possibility that our data do not include unreported cases of pediatric mushroom poisoning with hepatotoxic effects or other severe outcomes. Future research in this area should focus on prospectively collecting data and pooling results among several centers to obtain more meaningful numbers.

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COMMENTARY

The optimal management of mushroom poisoning remains undetermined

> I have heard of a physician of Mysia who administered Fowl's dung to persons suffering from fungus poisoning, and I myself have experimented with the remedy. I have used finely powdered dung mixed with water or mixed with honey and vinegar. The patients immediately on drinking the mixture vomited and recovered. One must observe that the dung of a fowl at liberty is more efficacious than one in confinement.
>
> *De simplicium medicamentorum temperamentis et facultatibus*
>
> GALEN, CA AD 150

Although the treatment of patients exposed to toxic mushrooms has become somewhat more sophisticated since Galen first extolled the advantages of free-range chicken,[1(pp39-40)] the ideal management of these cases has still not been determined. Problems arise because often the clinical history is unclear, the precise mushroom or mushrooms involved are unidentified, or the diagnosis is unsuspected in a patient who presents with signs and symptoms of gastroenteritis. In addition, the various antidotes—such as silibinin and thioctic acid [lipoic acid]—proposed for treating exposure to the potentially fatal amatoxin-containing species have not been shown to improve outcome.

Some helpful information can be gleaned from studies previously published in the medical literature. Trestrail analyzed cases of mushroom exposure reported in 1989 to the National Data Collection System of the American Association of Poison Control Centers (AAPCC).[2] He found that of 9,208 total cases of exposure, the species involved was identified in only 3.4%. Most patients (81%) were younger than 6 years. Only 0.2% of the patients had major toxic manifestations, and the mortality rate was extremely low (0.03%). All 3 deaths involved amatoxin-containing species such as *Amanita phalloides.* The 1998 AAPCC data showed similar trends: 9,839 reported cases of exposure, with 69% involving children younger than 6 years. The species was identified in only 12% of cases, with only 1 death.[3]

The retrospective study by Nordt and colleagues of cases of mushroom exposure reported to the AAPCC during the years 1993 through 1997 from California had results consistent with those of previous reports. The single death in the 6,317 cases surveyed involved an adult who ate foraged mushrooms. Recent literature suggests that almost all deaths in these cases arise from similar scenarios: adults making a meal of foraged wild mushrooms.[4-8] Often the victims are immigrants who do not realize that mycologic expertise developed in their native lands may not hold up among the unfamiliar species of the United States. Deaths of children who inadvertently ingest a mushroom while "grazing" outdoors seem to be exceedingly rare, if they occur at all. I was unable to find any such case reported in the recent medical literature.

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Deciding on the optimal management approach when faced with a case in which a fatal outcome is possible but unlikely is always difficult. In patients with mushroom exposure, suspicion should be heightened and management more aggressive when gastrointestinal symptoms begin more than 6 hours after ingestion or when the patient reports eating a meal of foraged mushrooms. Identifying the exact species involved would be ideal, but often no specimen is provided or no expert mycologist is available. Computerized mushroom identification systems have not proved to be reliable.[9] Severe gastrointestinal manifestations should be treated aggressively with volume replacement and cardiovascular support. Patients suspected of having ingested amatoxin-containing mushrooms should be observed (as an outpatient or inpatient) at least daily for 72 hours for recurrent symptoms, elevated liver enzyme levels, hypoglycemia, acidosis, and coagulopathy.

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On telling the truth to patients with dementia

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ABSTRACT **Objectives** To discover what dementia sufferers think is wrong with them, what they have been told and by whom, and what they wish to know about their illness. **Background** Ethical guidelines regarding telling truth appear to be equivocal. Declarations of cognitively intact subjects, attitudes of family members, and current psychiatric practice all vary, but no previous research has been published concerning what patients with dementia would like to know about their diagnosis and prognosis. **Design** Questionnaire study of patients' opinions. **Setting** Old Age Psychiatry Service in Worcester, United Kingdom. **Participants** Thirty consecutive patients with dementia. **Results** The quality of information received has been poor, and many patients have no opportunity to discuss their illness with anybody. Despite that, almost half of the participants in this study had adequate insight, and most declared that they would like to know more about their predicament. **Conclusions** Although many patients would like to know the truth, the rights of those who do not want to know should also be respected. Therefore, the diagnosis of dementia should not be routinely disclosed, but just as in other disorders, health care professionals should seek to understand their patients' preferences and act appropriately according to their choice.

INTRODUCTION

Dementia is a syndrome, usually of a chronic and progressive nature, in which there is decline of cognitive functions, accompanied by deterioration in emotional control, language skills, and social behavior. It occurs in Alzheimer disease, cerebrovascular disorders, and other conditions primarily or secondarily affecting the brain. Although dementia may begin at any age, most frequently it affects elderly persons, particularly after age 75 years. In most cases, its course is irreversible; despite significant progress, no effective treatment is currently available. Trying to help people with dementia is not only a challenge to physicians' professional skills but also confronts us with difficult questions about the limits of individual autonomy and medical paternalism, the dignity of persons, and their best interests.

In this article, I address an apparently simple problem concerning the giving of diagnostic information to people with dementia. A recent survey of old age psychiatry consultants showed that most of them "rarely" or only "sometimes" informed their patients about the diagnosis and almost never about the prognosis. Providing information seemed to depend on the level of impairment. In all, 38%

of consultants "nearly always" informed patients with mild dementia, but in those with moderate and severe dementia, only 13% and 6%, respectively, discussed the diagnosis with their patients. However, 98% of the respondents "nearly always" informed patients' families and carers about the diagnosis and prognosis.[1] Similar practice has been observed among geriatricians, although they tend to tell their patients with mild dementia more and their carers less than psychiatrists do.[2]

Most (57%-83%) relatives of dementia sufferers do not want the patient to be told the diagnosis, but more than 70% of the relatives would want to be told the truth if they had the disorder themselves.[3,4] However, in cases where the diagnosis had been given, most of the carers found it helpful both for themselves (98%) and for the patients (84%).[5] Only 1 study attempted to elicit patients' preferences. When attendees at 2 primary care practices were presented with a vignette of a patient with Alzheimer disease, most (92%) declared they would like to know the truth. Almost the same proportion (87%) stated that members of their families or friends should have been fully informed. However, the participants in this study were cognitively intact, and almost half of them were younger than 50 years.[6] I am not aware of any published study exploring the wishes and preferences of patients with dementia, and therefore, I undertook this inquiry.

WHAT DO PATIENTS WITH DEMENTIA WANT TO KNOW?

My aim was to explore what the patients think is wrong with them, whether and what they have been told by their physicians about their condition, and what they would like to know about their illness. Thirty consecutive patients seen by me between October and December 1997 in the Old Age Psychiatry Service in Worcester participated in the study. Twenty were women. The patients ranged in age from 63 to 92 years (mean, 81 years). At the time of examination, 11 participants were inpatients, and 19 were outpatients. They had been in contact with the psychiatric service from 1 day to 17 years (mean, 1 year 10 months). All had a clinical diagnosis of dementia based on *International Classification of Diseases, 10th Revision* (ICD-10) criteria,[7] including Alzheimer disease (n = 11), vascular dementia (n = 9), and other or unspecified dementias (n = 10). In addition, consensus guidelines were used to make a diagnosis of dementia with Lewy bodies in 1 of the otherwise unspecified dementias.[8] Participants' cognitive states were assessed using the Mini-Mental State Examination[9]; scores ranged from 7 to 29 (median = 18, and mean = 18). All participants gave verbal consent and answered a set of standard questions regarding the information they had received about their illness (the questionnaire is available from the author on request). The answers were recorded verbatim and will be the subject of further analysis.

INSIGHT:

"What do you think is wrong with you?"

I assumed that the participants had adequate insight if they were able to give the correct diagnosis or, at least, to describe adequately their main symptoms. Of the 30 participants, 14 (47%) fulfilled these criteria. Most complained of problems with memory. No participant used the word "dementia," but a few were able to accurately describe their conditions. Examples are shown in the first box.

The rest of the participants (16/30) either denied any problems or gave implausible explanations for their predicaments, such as: "loneliness," "old age," "stomach upset," and the like. Four patients simply said "don't know" without further elaboration.

"What have you been told about your illness?"

Of the 30 participants, 20 reported that nobody had ever talked with them about their illness. Only 5 had had an opportunity to discuss it with their physicians. Sometimes the information was provided by nurses (3 participants) and friends (2 participants) but never by the family members. Only 1 participant said that she had been told her diagnosis. In 2 cases, the professionals attempted to reassure the patients ("There is not much wrong with you") and advised them to take prescribed medication. Three participants reported clearly untrue explanations allegedly given by their physicians: hearing impairment, angina pectoris, and bereavement had been suggested as responsible for their present conditions. Two participants declared that the content of the information they were given was insulting ("She told me I was mad," and "She said I was completely out of my balls and very needful"). Two participants either did not remember or could not understand what the informers had been trying to tell them.

"What would you like to know?"

Most of the participants with dementia (21/30) declared they would like to know what was wrong with them or wished to get more information if they already knew. Ten wanted to know their diagnoses, 5 were interested in the possibility of improvement, and 1 wished to know more

Patients' expressions of their condition*

- "I had a stroke. I am not very bright after that, and I cannot do things as I used to" (vascular dementia: MMSE 15)
- "I do not really know what is wrong with me, but I have problems with my memory and hallucinations" (dementia with Lewy bodies: MMSE 12)
- "I am not very clear in my understanding" (Alzheimer disease: MMSE 7)

*Numbers in parentheses indicate the score on the Mini-Mental State Examination (MMSE).

about the causes of the disorder. Sometimes they could not specify what exactly they would like to know (4 participants), but some of their questions might have been difficult to answer, for example: "Why me?" or "How long will I suffer?"

Where the participants specified whom they would wish to give them information about their illnesses, most (8/12) preferred that it should be their physician. Only rarely did patients feel that they should receive the information from other persons such as family members (2 participants) or anybody with adequate knowledge (2 participants).

Patient who does not want to know

Nine participants (30%) did not want to know what was wrong with them or to receive any information about their illness. Although we did not asked them why, some of them spontaneously tried to explain their choice. Their motives seem to display a wide spectrum from probably full insight through more or less conscious decisions not to know the truth to complete denial of their illness (see second box).

I could not find any clinical or demographic characteristics indicating those who would prefer to be told from those who would not.

DISCUSSION

Dementia and the problem of truth-telling

Methodologic limitations of the study may reduce the credibility of its results. The study has been based only on the declarations of patients, without attempting to verify them by their therapists or to compare them with the information given to carers. The subjects were cognitively impaired and because of the memory deficits, might not have been able to recall what they had been told. In the milder cases, the cognitive decline may be seriously threatening for many patients. To cope with the anxiety and to maintain their self-esteem, they might use various psychological defense mechanisms, such as denial and minimalization of the impairments, avoidance in discussing the problem, or vagueness and circumstantiality when forced to do so.[10] Such defense mechanisms may render their statements less accurate, as has frequently been observed in other disorders—even in many terminally ill patients who have been told their diagnosis but simply deny they have been told.[11] However, almost half of the participants with dementia had satisfactory insight, and 21 (70%) clearly declared they would like to know more about their illness. When in a parallel inquiry their statements were compared with those of cognitively intact peers with functional (predominantly depressive) disorders, no significant differences were found in the quality of received information, level of insight or the proportion of those willing to know about the illness (D Battin and M Marzanski, unpublished data). Of course, this is a small study from only 1 old age psychiatry service, so results of similar studies elsewhere might differ. However, the self-reported reluctance of physicians from other centers to disclose information about diagnosis to dementia sufferers strongly suggests that the pattern in Worcester is not unique.

Ethical codes and telling the diagnosis

Moreover, in the codes of medical ethics, the guidelines regarding disclosure of diagnosis are equivocal and may be interpreted in various ways. In the Hippocratic Oath, nothing about telling truth is explicitly stated. Nevertheless, even here a conflict exists between difficult-to-reconcile demands. Physicians should practice their art with purity and holiness, which may imply veracity; on the other hand, they should follow only that system or regimen that they consider beneficial to their patients, and they should abstain from anything that is deleterious and mischievous. Of course, the truth about dementia may be deleterious, mischievous, and devastating. A modern restatement of the Hippocratic Oath, known as the Declaration of Geneva (1947), seems to ignore the problem of veracity, stating simply that the health of the patient should be the physician's first consideration. The International Code of Medical Ethics (1968 and 1983) demands that a physician deal honestly with patients and colleagues, but this concerns competence and professional misconduct, rather than telling patients what is wrong with them. In the Declaration of Lisbon (1981), the World Medical Association stated: "The patient has the right to accept or refuse treatment after receiving adequate information."[12] This may suggest that telling the truth about diagnoses is a mere prerequisite to the choice of treatment. This impression seems to be reinforced in the ethical guidelines for the psychiatric profession. The World Psychiatric Association's Declaration of Hawaii (1977 and 1983) says[13]:

> The psychiatrist should inform the patient of the nature of the condition, therapeutic procedures, including pos-

Patients' denial of dementia*

- "I already know what it is" (vascular dementia: MMSE 15)
- "I can't remember things, but I don't think anything is wrong about that" (Alzheimer disease: MMSE 16)
- "There is no point in talking unless you can improve it, but you can't, can you?" (Alzheimer disease: MMSE 23)
- "I have enough troubles" (vascular dementia: MMSE 28)
- "I don't really want to know what is wrong with me" (Alzheimer disease: MMSE 18)
- "I would like to know if I was ill, but I am not" (unspecified dementia: MMSE 24)

*Numbers in parentheses indicate the score on the Mini-Mental State Examination (MMSE).

sible alternatives, and of the possible outcome. This information must be offered in a considerate way, and the patient must be given the opportunity to choose between appropriate and available methods.

But does this mean that psychiatrists have the duty to provide the information when there is no treatment? And how truthful should be the "considerate way"? Does it imply the whole truth? As much as the patient wants? As much as the patient's physician believes is sufficient? The General Medical Council (1995) recommends that physicians, to establish and maintain trust in their relationships with patients, must give them "the information they ask for or need about their condition, its treatment and prognosis . . . in a way they can understand."[14(p4)] In practice, patients with dementia rarely ask for the information, and many physicians seem to think that because there is no cure to offer, such knowledge may be only detrimental and, therefore, not needed in therapeutic relationships. But can the relationships be successful without telling the truth?

Ethical theories and telling the diagnosis

Two schools of ethical thought address these dilemmas. Deontology (study of the field of professional ethics and duties) assumes that lying and deception are wrong in themselves and that clinicians, like everyone else, have a moral duty to tell the truth. Competent patients have a right to know their diagnosis; this information belongs to them, and they should be told the truth regardless of the consequences. Consequentialism insists that the decision to tell or not to tell depends on the details of the clinical situation, and the physician should decide which course of action might be least harmful and produce the best results for the patient.

In the deontologic approach, the word "competent" may cause reservations—it is difficult to understand why any illness might deprive the sufferer of the right to know about it. Competence is usually defined with respect to a particular task or performance, and the only relevant skill here is that of being able to "take in" diagnostic information. At the moment, the most prominent advocates of truth-telling seem to think that the nature and degree of the disease may limit the right to information. Pitt claims that "although there is probably no point in telling those whose Alzheimer's disease is so advanced that they cannot understand their diagnosis, in all other cases the right of those who have presented as patients, to know what is thought to be wrong with them should be respected."[15] But it remains controversial when, if ever, a person loses that right and whether incompetence (defined by others as inability to understand diagnostic information) is enough.

Regarding the consequentialist view, it might be argued that in doctor-patient relationships, nothing is more difficult to predict than the outcome of our own predictions. Physicians commonly tend to attribute their own fears and hopes to the patients—surprisingly often, the patients do not meet those expectations. In the 1950s, 90% of physicians did not inform their patients about the diagnosis of cancer.[16] One of the early arguments for disclosure was the availability of radiotherapy and chemotherapy, which could alter the course of the disease. The need for a patient's consent to initiate such treatment outweighed previous concerns about possible harm associated with breaking the bad news. Only subsequently has it been proved that most patients want to know their diagnosis and its consequences, and now 97% of physicians tell their patients about the nature of the disease.[17] Perhaps a similar change of attitudes will occur in old age psychiatry after the introduction of the new "antidementia" drugs, and appeals in this direction have already been launched.[18,19] Today, the attitudes and practice of old age psychiatrists remain different from those of their colleagues from other specialties. Even in patients with schizophrenia and those with affective disorders, psychiatrists tend to inform their patients much more frequently—58% and 90%, respectively.[20]

Arguments in favor of truth-telling

According to Beauchamp and Childress,[21] the main arguments obligating veracity are the following.

Respect for autonomy

Lies and deceit breach the autonomy of a person.[22] Patients cannot make valid decisions unless they are fully informed. That usually involves informed consent to treatment, but of course, other decisions need to be made regarding legal aid, driving, finances, and planning for the future. The argument is not as obvious in patients with profound dementia who are no longer competent free agents and whose self-governance may be seriously limited. Agich has argued that the liberal concept of autonomy, which stresses independence and freedom from interference from others, is neither appropriate nor suitable here.[23] Respect for the autonomy of dementia sufferers entails a commitment to identify and establish the conditions necessary to continue their lives in the way they are still able to and as closely as possible to the way they have normally lived. Such a commitment should involve hope resulting, in Agich's view, from meaningful relations with others. Could delivery of the devastating truth serve them better than not telling the truth?

Need for trust in doctor-patient relationship

Mutual trust cannot be built on deception and lies. In addition, concealment, even with good intentions, once started, probably would have to be continued. Its escalation might easily lead to abuse and harm of those not fit

enough to be informed by those who can manipulate them according to their own needs and beliefs. On the other hand, therapeutic relationships in severe dementia may be difficult or impossible to establish, and the professionals often seem to work rather for the carers than directly for the patients. It seems also to be true that many close relations have been threatened or destroyed by too much candor.

Acknowledgment of reciprocal obligations, fidelity, and promise keeping

Any social contract involves mutual rights and obligations. In therapy, the contract concerns specifically the patient's health and should include the right to honest information about diagnosis and prognosis. However, many patients with dementia arguably are not able to enter any social contract simply as a direct result of their cognitive impairment, and the primary obligation of their physicians remains the principle "not to harm." It has also been claimed that physicians, like everyone else, have a duty not to lie but are not duty-bound to avoid deception.[24]

Arguments for limited truth-telling or lying

Arguments for limited disclosure and deception quoted by Beauchamp and Childress[21] include the following.

Therapeutic privilege

Honesty should not be confused with cruel openness,[25] and if disclosure of the information seems to be harmful to the patient, the physician may be justified in withholding the information or even in using benevolent deception. The therapeutic privilege has a long tradition in medical practice, although more recently it has been criticized as an example of unacceptable paternalism. Misleading the patient contributes to the cult of expertise surrounding the medical profession and to a view of physicians not as providing a service, but as guardians of a special wisdom that they may determine when, and to whom, to divulge.[26] However, paternalism frequently appears to be unavoidable in dementia care, and some professionals still defend telling lies to cognitively impaired patients.[27] After all, anxiety, depression, and catastrophic and psychotic reactions do occur as the result of disclosure,[28] and even suicides committed by patients unable to live with the burden have been reported.[29]

Patients are not able to understand the information

A convincing excuse for not disclosing the diagnosis is when patients have difficulties in acquiring new information complicated by memory deficits, impaired use of language, and inability to understand abstract concepts. But it may be argued that just because of the nature of dementia, patients should know well in advance about the threats to their intellectual functioning. They experience their illness and deserve an explanation of what is happening to them. Moreover, cognitive deficits do not remove their right to know the truth—they only make it more difficult for the physician to provide understandable information to the patient. Lying and deceiving seem to deny them due respect and degrade their dignity. As in any other group of disorders, patients with dementia require affirmation because they are persons, not just because they have been examined and found rational and competent. The truth may be neither fully understood nor remembered by the patient and difficult for the physician, but neither of these problems should remove the obligation to be honest and truthful.

Dennis Cook/AP

Ronald Reagan in 1987, 7 years before the public announcement that he had Alzheimer disease. Did his physicians discuss the diagnosis with him?

Some patients do not want to know the truth about their condition

Besides the right to know, there is also the right not to know. Patients may prefer to ignore the truth completely or to select only those parts of it that they want to know. If we accept that physicians ought to respect their patients' wishes, then the important issue is not what family members, other patients, or professionals think, but what the patient in the particular circumstances wants.[30] In my study, a substantial proportion of the participants (30%) preferred not to be informed about their illness, and their motives seemed to be diverse. This requires careful attention from health care professionals, who should not force unwanted information on patients but should seek to understand their patients' preferences and act according to their choices.

CONCLUSIONS

Veracity appears to be a difficult virtue and a difficult-to-fulfill obligation. Reconciling conflicting principles and judging how much information a patient should be given are not easy. Additional ambiguities may arise because of the difficult, sometimes impossible, task of balancing autonomy and paternalism. A review of the literature shows

that in dementia, it is also unclear whether knowing the truth about one's health is the right of the person or a privilege available to those who are sufficiently bright to understand the information, brave enough to request it explicitly, and strong enough to cope with its burden. My study suggests that we ought to ask patients with dementia whether they wish to know more about their diagnosis. Each patient must be approached individually and his or her choices respected, whatever the level of impairment. Furthermore, having discussed the diagnosis once, the physician may need to go over it again, which implies that physicians must have the requisite communication skills to provide information in various ways. However, the effect of telling or not telling patients with dementia their diagnosis remains unknown and requires a further prospective study.

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COMMENTARY

The treacherous path of truth-telling with demented patients

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Research in dementia has never been more intensive as we approach a better understanding of the dominant form of dementia, Alzheimer disease, through scientific work with transgenic mouse models, vaccine trials, gene localization, and new technologies for early recognition. Although we are still in the early investigative stages, it may not be long before genetic testing and neuroradiologic tests will provide unimpaired persons with reliable information about their likelihood of developing Alzheimer disease.[1] There will be important ethical issues concerning the role of premorbid diagnoses, as there are issues now about disclosing the diagnosis of dementia to symptomatic patients.

Marzanski addresses the latter concern and highlights

an important and challenging clinical area—appropriate and effective communication with dementia sufferers. The question of whether there is adequate disclosure of information to patients regarding their diagnosis of dementia is explored in a survey of 30 consecutive patients with dementia. Fourteen of 30 patients appeared to have adequate insight by Dr Marzanski's criteria, based on the ability to correctly state their diagnosis or describe their symptoms. Twenty reported that no one had ever talked to them about their illness, and a similar number (21/30) desired more information.

Estimating the reliability of responses from cognitively impaired patients is a formidable challenge. Without more detailed information about cognitive assessment, beyond the MMSE, few conclusions can be drawn regarding how these responses relate to the content and quality of communication with their physicians. We do not know—from what is reported—how many of those who desired more information also met criteria for adequate insight. Nor do we know whether the type of impairment and level of severity influenced the responses.

Although this study design does not evaluate the quality and quantity of physician disclosure about dementia, the struggle of how to discuss dementia with patients and caregivers resonates for all physicians caring for older patients. The presence of sensitive and honest discussion about dementia may, in fact, be a quality indicator of caring for older patients. It reflects a level of effective communication and psychosocial therapeutics administered by health care professionals to older patients. In citing the work of Novak and colleagues,[2] Marzanski aptly draws parallels between this issue and truth-telling about cancer. The cognitive dissonance for physicians is similar here. The fear of facing loss and death in our patients and, thus, in ourselves can be inhibitory, and medical school curricula likely still have some distance to travel before all physicians are appropriately trained in effective and appropriate communication regarding these issues.[3] This distance is even greater when considering sensitive communication with those who are cognitively impaired.

We might assume that several of the patients in Marzanski's study had moderate to severe dementia. This assumption is based on what we know about US medical practice. Patients are not typically recognized as cognitively impaired before they are moderately to severely affected.[4] Furthermore, even among patients with moderate to severe forms of impairment, only 25% are likely recognized by physicians as having dementia.[5] Dementia is not usually identified in earlier stages without formal cognitive testing, and cognitive screening tests are performed infrequently in general clinical practice in the United States.[6] The reasons for inadequate recognition likely include the lack of appropriate training, reinforced by a sense of therapeutic nihilism about treatment. Such barriers may explain why there is less than full disclosure with patients about their diagnosis and prognosis, and these may have been present in Marzanski's study. Possible barriers to appropriate discussions include a reasonable estimation that impaired comprehension will limit the meaningfulness of discussions. This is further justification for an earlier diagnosis because the best time to discuss life-altering and life-threatening disease is when patients can remember the conversation, understand its significance, and participate in health care decisions.

Marzanski identifies a substantial limitation in his study design: the lack of verification from caregivers and physicians that these patients were never told about their diagnosis. Despite that concern, there is other evidence that the picture is not always bleak in terms of patients being given diagnostic information. One study conducted in the United Kingdom explored the issue of disclosure through surveys of 20 memory disorders clinics.[7] Six of 16 who returned questionnaires had policies for sharing diagnoses, and staff members generally perceived themselves as speaking openly, yet sensitively, about diagnoses.

Marzanski leaves us with more questions than answers. This is appropriate for exploratory research. This study should cause health care professionals to stop and think about how they handle the issue of truth-telling with dementia sufferers and their families. If such pause occurs, Marzanski has helped us take an important step toward improving care for those with dementia.

Joshua Chodosh recently completed a research fellowship at UCLA School of Medicine as a Robert Wood Johnson/Veterans Affairs Clinical Scholar.

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Screening travelers for hepatitis A antibodies

An observational cost-comparison study of vaccine use

ABSTRACT **Objectives** To measure the seroprevalence of antibodies to hepatitis A virus (anti-HAV) in a health plan population of travelers and to determine whether prevaccination screening for anti-HAV can reduce unnecessary vaccination and thus promote the most effective, economic use of hepatitis A vaccine. **Design** Observational, cost-comparison study. **Setting** Central injection clinic of a health maintenance organization medical center. **Subjects** Five hundred twenty-seven adults who denied having previous hepatitis A or vaccination. **Main outcome measures** Subgroups with the greatest prevalence of anti-HAV seen between June 1995 and April 1996 for immunizations before traveling to nonindustrialized countries. Relative costs of their screening and immunization. **Results** The presence of anti-HAV precluded the need for vaccination in 148 subjects (28.1%). The highest prevalence of anti-HAV (82.7%) was found in subjects born in nonindustrialized countries (62/75), in subjects who had previously traveled to areas of endemic hepatitis A (32.1% [135/420]), and in subjects born before 1945 (29.2% [92/315]). Costs of screening and vaccinating travelers were cheapest if prevaccination antibody sera testing was limited to subjects born in nonindustrialized countries and those born before 1945. **Conclusions** Prevaccination screening of travelers for hepatitis A can be done selectively on the basis of age and country of origin. This strategy could lead to a more economic use of the vaccine and clinic resources.

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INTRODUCTION

Travelers to nonindustrialized countries or to areas endemic for hepatitis A virus (HAV) are at risk for contracting hepatitis A, primarily through contact with contaminated food or water. For frequent or long-term travelers, the new hepatitis A vaccine provides longer-lasting protection than immune serum globulin (ISG),[1] which was previously the only prophylactic medication available to travelers to areas of endemic hepatitis A. The vaccine provides much higher antibody titers and much longer-lasting protection than that provided by ISG.

The symptoms of HAV infection are often mild or unnoticed. Therefore, the true prevalence of HAV infection is difficult to determine.[2] Previous research has identified specific groups of people who are more likely to have antibodies to HAV (anti-HAV). In nonindustrialized countries, HAV infection occurs frequently in children and is typically mild or asymptomatic.[2] Almost all children in areas of highly endemic HAV have anti-HAV before age 10 years.[3,4] Thus, people born in nonindustrialized countries have a higher prevalence of anti-HAV than the general US population.[4,5] Moreover, because sanitation in the United States and in other industrialized nations has improved during the past half century, the prevalence of anti-HAV is higher in older people and lower in those born in the past 30 to 40 years.[6] In industrialized nations, persons aged 51 years or older have historically had the highest seroprevalence rates of anti-HAV: 50% to 60% of the population aged 51 years or older test positive for anti-HAV in serum specimens.[4] In a 3-month pilot study conducted at Kaiser Permanente Medical Center in Denver, Colorado, during 1996, travelers were screened for anti-HAV.[7] Of the 49 seropositive patients found, 22 (45%) were born outside the United States, and 26 (96%) of the 27 remaining seropositive patients were aged 55 years or older.[7] Travelers to areas of endemic hepatitis A, particularly those who deviate from normal tourist routes, can also be presumed to have a higher incidence of anti-HAV.[1]

We undertook this study to ascertain the seroprevalence of anti-HAV in our health maintenance organization (HMO) population by examining factors other than age alone. After groups with the highest incidence of anti-HAV are identified, methods to implement selective prevaccination screening could be developed to reduce unnecessary vaccination.

METHODS

Kaiser Permanente Medical Center in Sacramento, California, is a staff-model HMO facility that provides care to more than 500,000 Kaiser Foundation Health Plan members who live in the surrounding area. All members of this health plan who travel outside the country receive information and immunizations at an adult injection clinic supervised by 2 registered nurses in consultation with a physician specializing in infectious disease. With the use of a prospective questionnaire administered in the injection clinic from June 1995 through April 1996, travel medicine needs were evaluated for 527 members from ages 18 through 82 years who were traveling to nonindustrialized

countries. This pilot work was used to devise a strategy for the most economic use of hepatitis A vaccine.

On the basis of questionnaire responses, travelers were categorized by age, country of origin, vaccination history, and previous travel experience. Only travelers who denied having previous vaccination with hepatitis A vaccine, known infection with HAV, or injection with ISG within the previous 6 months were included in the study. Before vaccination, travelers were screened for IgG anti-HAV levels using an enzyme immunoassay. Hepatitis A vaccine was administered to those who were not immune. Pediatric patients, travelers who elected not to use our travel clinic, and those who chose not to participate in the study were excluded from our analysis. Travelers to industrialized countries were excluded from this study, and 6 travelers were excluded because they were leaving the country before test results could be received. All of these excluded travelers could conceivably have a different anti-HAV profile than our study participants.

We compared the cost of prevaccination screening in subjects who lacked immunity. This cost analysis included 2 options: screening all travelers without categorizing them into subgroups and vaccinating all travelers without conducting prevaccination screening. The cost of the antibody test was estimated to be $7.00, and the mean wholesale price of 2 doses of HAV vaccine was estimated to be $118.90[8]: Estimated clinic personnel costs were based on a time requirement of 10 minutes per test (patient education, preparing laboratory slips, drawing blood specimens, and notifying patients of results reported in 2-3 days) at our organization's fully benefited contract rate of $35.00 per hour for registered nurses. The benefits include coverage for health and dental insurance, vacation pay, sick pay, and holiday pay in addition to hourly compensation.

Table 1 *Prevalence of antibodies to hepatitis A virus (anti-HAV) in 527 travelers screened at a central injection clinic of a health maintenance organization*

Group characteristics	No. of subjects tested	No. (%) of subjects positive for anti-HAV
Age, yr		
Overall*	527	146 (27.7)
18-50 (ie, born after 1945)	212	54 (25.5)
≥51 (ie, born in 1945 or earlier)	315	92 (29.2)
Born in nonindustrialized country†	75	62 (82.7)
Previously traveled to areas of endemic hepatitis A	420	135 (32.1)
Born in industrialized country		
Overall	428	71 (16.6)
Age 18-50 yr (ie, born after 1945)‡	158	10 (6.3)
≥51 yr (ie, born in 1945 or earlier)	270	61 (22.6)

*Includes patients who did not fit measures of other groups because of indefinite birth history.
†Includes 1 subject each from Spain, Venezuela, Iran, Tanzania, Rwanda, Zambia, Mexico, and Thailand; 2 from Peru; 3 each from Yugoslavia and unspecified African countries; 6 from Philippines; 12 each from China and Vietnam or Cambodia; and 29 from India.
‡Includes 1 subject each from Netherlands and Sweden; 2 each from Australia, Canada, Scotland, and Germany; 3 each from England, Japan, and Ireland; and 139 from United States.

RESULTS

Specific subgroups had a higher rate of HAV immunity than other groups (table 1). Of 527 travelers whose questionnaire responses noted travel to nonindustrialized countries, 75 were born in nonindustrialized countries; of these 75 travelers, 62 (82.7%) had HAV immunity—the highest overall rate of any group, regardless of age. In comparison, only 71 (16.6%) of 428 travelers born in industrialized countries showed immunity to HAV. However, when this group of travelers was categorized by age, the percentage of HAV immunity was even lower than the 17% rate for travelers aged 50 years or younger who were born in industrialized countries. Of the 158 travelers in this category, 10 (6.3%) had anti-HAV. For travelers aged 51 years or older who were born in industrialized countries, the percentage was higher than the 17% rate for all travelers born in nonindustrialized countries. Of the 270 travelers in this category, 61 (22.6%) had anti-HAV. A large percentage (80.0%) of the 527 travelers responding to the questionnaire had previously traveled to areas of endemic hepatitis A, and 135 (32.1%) of these 420 subjects showed HAV immunity. Screening by age alone was not as good a predictor of HAV immunity as other indicators. HAV immunity was found in 54 (25.5%) subjects aged 18 through 50 years and in 92 (29.2%) subjects aged 51 years or older.

Combining travelers aged 51 years or older and those born after 1945 in a nonindustrialized country yielded a group that had the highest prevalence of anti-HAV (table 2).[8] The calculated cost for screening and immunizing the seronegative subjects in this group was $52,481, or $99.58 per traveler seen. The next cheapest strategy (prevaccination screening of all travelers with subsequent immunization as needed) was calculated to cost $54,276, or $102.99 per traveler. The third cheapest strategy (screen and immunize those who had traveled to areas where hepatitis A was endemic) was calculated to cost $54,284, or $103.01 per traveler seen. Screening travelers aged 18 through 50 years who were born in industrialized countries was calculated to cost $66,512, or $126.21 per traveler seen. Vaccination of all patients without any prevaccination screening was calculated to cost $65,732, or $124.73 per traveler seen. The cost difference between the cheapest screening strategy and the most expensive screening strategy was $14,031, or $26.63 per traveler seen; and the difference in cost between the cheapest strategy and the strategy of vaccinating all travelers without any prevaccination screening was $13,251, or $25.15 per traveler seen. The difference in cost between the cheapest strategy and

Table 2 *Cost comparison (in 1996 $US) of prevaccination strategies for screening 527 members of a health maintenance organization for anti-HAV*

Subgroup screened (No. subjects)	Laboratory cost of screening, $*	Personnel cost of screening, $†	Cost of vaccine‡ (No. subjects vaccinated), $§	Personnel cost of vaccine administration, $‖	Total cost, $	Cost of strategy per traveler seen, $	Cost ranking of screening strategy¶
None; vaccination only (527)	NA	NA	62,660 (527)	3,072	65,732	124.73	9
All (527)	3,680	3,074	45,301 (381)	2,221	54,276	102.99	2
Age 18-50 yr (212)	1,484	1,237	56,240 (473)	2,758	61,719	117.11	7
Born after 1945 in industrialized country (158)	1,106	921	61,471 (517)	3,014	66,512	126.21	10
Born after 1945 in a nonindustrialized country (52)	364	303	57,429 (483)	2,816	60,912	115.58	5
Age ≥51 yr (315)	2,205	1,838	51,721 (435)	2,536	58,300	110.63	4
Born in 1945 or earlier in industrialized country (270)	1,890	1,575	55,407 (466)	2,717	61,589	116.87	6
Born in 1945 or earlier in nonindustrialized country (23)	161	134	60,520 (509)	2,967	63,782	121.03	8
Age ≥51 yr or born after 1945 in nonindustrialized country (367)	2,569	2,140	45,539 (383)	2,233	52,481	99.58	1
Previously traveled to area of endemic hepatitis A (420)	2,940	2,450	46,609 (392)	2,285	54,284	103.01	3

NA = not applicable.
*Based on Kaiser Permanente Regional Laboratory, Berkeley, California, cost of $7.00 per test and 5 minutes of personnel time to draw the specimen at fully benefited cost.
†Additional personnel cost based on 10 minutes per test (explain to patient, prepare laboratory slips, review results, notify patient of results) at fully benefited cost of $35.00 per hour.
‡Based on mean wholesale cost of $59.45 per injection (Havrix vaccine; SmithKline Beecham Biologicals, Rixensart, Belgium)[8]; 2-shot series administered in 6 to 12 months.
§Subgroup members who tested negative for anti-HAV plus others who were vaccinated presumptively and were not tested.
‖Based on time estimate of 5 minutes per injection (including registration time) at $35.00 per hour.
¶1 = least costly, and 10 = most costly.

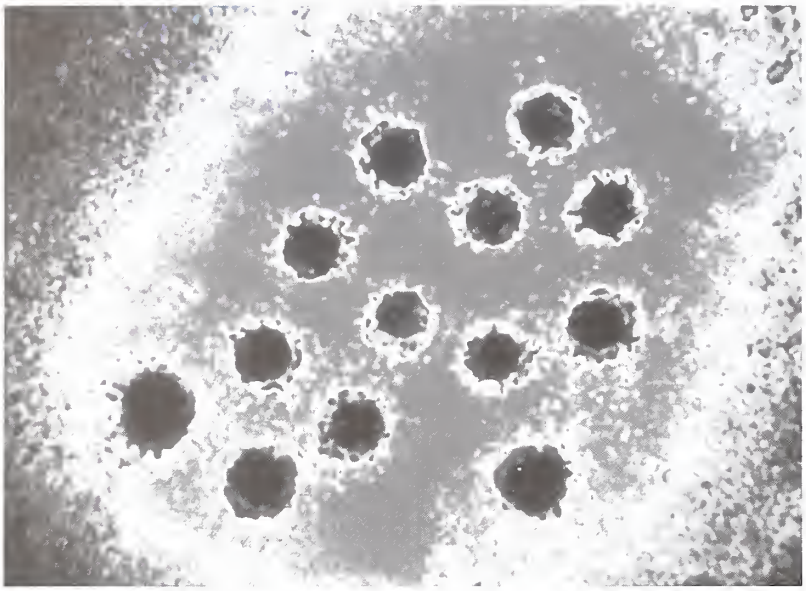
the strategy of screening all travelers was $1,795, or $3.41 per traveler seen.

DISCUSSION

The HAV vaccine is safe and effective: response rates as high as 99% to 100% after 2 doses have been reported,[9,10] and the vaccine has shown an exceptional safety profile.[11] Hepatitis A vaccine may provide protection for at least 20 years[5] and is the preferred method of prophylaxis for frequent or long-term travelers. Because medicine has become increasingly cost-conscious, most medical organizations would seek a vaccine that effectively prevents morbidity while minimizing costs and unnecessary vaccination.

The prevalence of anti-HAV varies widely among socioeconomic groups, even within the same geographic area.[2,12] Travelers to nonindustrialized countries risk exposure to hepatitis A, which can cause clinically significant morbidity.[13,14] Our study shows that prevaccination screening for anti-HAV may be useful for certain subgroups of travelers to nonindustrialized countries and that age alone is an insufficient variable for achieving the most cost-effective screening. Screening for anti-HAV in all travelers was less expensive than vaccinating all travelers without screening.

The cheapest strategy for providing vaccine to the study group was to selectively screen subgroups who had the highest rates of HAV immunity. In contrast, screening the group least likely to have anti-HAV was the most expensive way to carry out vaccination. After our screening program identified the subgroups of travelers who have the highest prevalence of anti-HAV, the cheapest strategy was to screen all travelers born before 1945 and those born in nonindustrialized countries after 1945. All other travelers were offered vaccination without screening because the incidence of anti-HAV in those travelers was low. No clinically significant adverse effects have been reported elsewhere in persons receiving the vaccine who have existing immunity to HAV.[5]



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The hepatitis A virus particles are prominent in this transmission electron micrograph

Only a small difference in cost per traveler was seen between the cheapest screening strategy and that of screening all travelers ($3.41). In a clinic such as ours with a high volume of travelers, selective screening can save money over time.

Given the difference in cost between administering vaccine without screening and administering vaccine with screening, one of the most expensive strategies in this analysis was to vaccinate all travelers without prevaccination screening. In addition, although traveler satisfaction was not directly measured in this study, the nurses operating the travel clinic reported an overwhelmingly positive response to the strategy of prevaccination screening. This positive response was especially true for travelers in the subgroups with a high prevalence of anti-HAV, in whom having a single blood test was preferable to receiving a series of 2 vaccinations. Avoiding unnecessary vaccinations and future trips to the clinic was highly desired by our travelers in general. Overall, travelers expressed high satisfaction when they were assured that they were already protected from HAV infection and that they, therefore, did not need the series of 2 vaccinations.

Our study assumes 100% compliance with the 2-injection vaccination series. However, even if the compliance rate for the second vaccination drops to as low as 50%, our cost ranking of screening strategies remains unchanged. A related observation is that, given 0% compliance with the second vaccination (ie, a single-injection vaccine series), the cost ranking of screening strategies changes so that the strategy of screening all travelers becomes slightly less expensive than screening all travelers born before 1945 and those born in nonindustrialized countries after 1945.

Another issue to consider is how the cost and effectiveness of using ISG for hepatitis A prevention compares with that of using the vaccine. The cost of ISG is about $28.72 per 2 mL.[8] The ISG vaccine provides protection for 3 to 6 months and is administered by the deep intramuscular route. The cost of both the ISG and the clinic visit needed to administer it would exceed the cost of 2 doses of HAV vaccine and their administration costs if a traveler went to nonindustrialized areas more than 4 times. The use of HAV vaccine for frequent travelers (travel abroad >4 times during a lifetime) would be more economical and would reduce the number of office visits needed by the traveler.

The cost of the vaccine is not expected to decrease greatly in the near future. However, how a change in vaccine cost would alter our cost ranking of screening strategies is a question that could be asked. On the basis of our cost assumptions, our recommended screening strategy would remain the most economic strategy, even with a 50% decrease in vaccine cost, and the most expensive strategy would remain so.

Another factor that could possibly affect our results is the effect of a less specific or less sensitive test for detecting anti-HAV. A more specific or a more sensitive test or 1 more specific and sensitive would not change our cost comparison. If the screening test is 10% less sensitive (ie, gives more false-negative results), the cost ranking of screening strategy remains unchanged for rankings 1 through 3. If the screening test is 10% less specific (ie, gives more false-positive results), then the strategy of screening travelers with previous travel to hepatitis A endemic areas becomes the least costly strategy, followed by the strategy of screening travelers 51 years or older or those born after 1945 in a nonindustrialized country.

Our findings and screening strategy may not be applicable to patient populations in other areas of the United States or in other industrialized nations because seroprevalence rates for anti-HAV may differ and because costs of vaccine and vaccine administration may also vary.

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COMMENTARY

Screening international travelers for hepatitis A antibodies versus routine vaccination: how generalizable are the results?

Lee and Blodget's results indicate that selective prevaccination screening of travelers can lead to cost savings compared with routinely using hepatitis A vaccine. They concluded that screening travelers aged 51 years or older and those born in nonindustrialized countries would save about $25 per traveler compared with routinely vaccinating all travelers. Aside from cost savings, travelers could benefit from screening for hepatitis A antibodies by needing fewer clinic visits and by avoiding adverse reactions to the vaccine.

Historically, many travel medicine clinics have been located within health departments and academic medical centers. Over time, primary care physicians and managed care organizations have also become sources of travel medicine services. As the authors imply, their study conducted within an HMO should be examined more closely to assess the representativeness of its patients and the ability to extrapolate the results to other travel medicine groups. Several questions immediately come to mind. First, what if hepatitis A vaccine costs are substantially lower than assumed by Lee and Blodget? Health departments and other state or federally administered travel medicine clinics generally are able to purchase vaccines at the lowest possible cost. Second, what if patient demographics vary markedly from those reported? For example, travel medicine patients attending a university-based clinic

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Table *Cost comparison of prevaccination screening strategies for hepatitis A antibodies among international travelers**

Screening strategy	Cost: Study results	Cost: Scenario 1†	Cost: Scenario 2†
No screening; vaccinate all patients	124.73	38.83	38.83
Screen all patients	102.99	40.91	41.44
Screen patients 18-50 years of age	117.11	40.02	41.11
Screen patients born after 1945 in an industrialized country	126.21	41.94	46.45
Screen patients born after 1945 in a nonindustrialized country	115.58	36.86	38.06
Screen patients 51 years of age or older	110.63	39.72	39.17
Screen patients born before 1945 in an industrialized country	116.87	40.91	39.71
Screen patients born before 1945 in a nonindustrialized country	121.03	38.07	38.63
Screen patients 51 years of age or older or born after 1945 in a nonindustrialized country	99.58	37.16	38.40
Screen patients who previously traveled to an area of endemic hepatitis A	103.01	39.11	39.11
Screen patients born in a nonindustrialized country‡	111.89	36.09	37.87

*Results represent total cost per traveler in dollars.
†See accompanying text for assumptions and methods.
‡This strategy was not presented in the study but results were computed using the reported data.

in the Southwest were younger than the study patients.[1] Third, what if fewer travelers are born in nonindustrialized countries than observed in the study?

Sensitivity analysis represents 1 approach to addressing these issues.[2] Although a comprehensive sensitivity analysis is not my intent, the table presents a comparison of the study results and 2 alternative scenarios. The first scenario represents a 1-way sensitivity analysis using the assumption of low vaccine cost to determine if hepatitis A antibody screening strategies remain preferable to routinely vaccinating all travelers (the 2-dose vaccine series may be purchased by a travel medicine clinic in the Southwest for slightly less than $33 vs about $119 in the study). Using higher vaccine costs than in the study would augment the cost savings attributed to the various screening strategies. The second scenario represents 1 aspect of a 3-way sensitivity analysis, again purposely making assumptions to test the robustness of the study results regarding cost savings attributed to screening for hepatitis A antibodies. The assumptions in this scenario are low vaccine cost (described above), a younger patient distribution[1] (22.7% older than 50 years vs 59.8% in the study), and a lower prevalence of travelers born in nonindustrialized countries (5.0% vs 14.2% in the study). In both scenarios, the remaining study variables and assumptions were unaltered and the percentages of positive hepatitis A antibody tests in each screened subgroup were assumed to remain unchanged. In addition, the strategy of screening only patients born in a nonindustrialized country was also tested.

Several findings are evident in the table. Both alternative scenarios resulted in substantially lower costs for all strategies, and the cost differences between strategies were greatly attenuated. Vaccinating all patients without screening costs less than most screening strategies in both scenarios. Interestingly, the strategy associated with the greatest cost savings was screening only patients born in a nonindustrialized country. Screening patients born after 1945 in an industrialized country consistently costs more than any other strategy.

What does this mean for physicians who counsel travelers? It certainly appears that screening for hepatitis A antibodies in various subgroups of patients may reduce the costs and possible risks associated with routinely vaccinating patients. Nevertheless, the cost savings may be substantially smaller than reported in the study, particularly in health departments or in other government-affiliated clinics. The heterogeneity of travelers across clinics and the many variables to be considered in cost-comparison studies suggest that a universally acceptable hepatitis A screening strategy will remain elusive. Regardless of whether screening is contemplated, it is imperative that travelers be advised to seek counseling at least 1 month before departure to ensure adequate vaccination for hepatitis A or other travel-related diseases, if needed.

Dr Licciardone is medical director of the International Travel Medicine Clinic at the University of North Texas Health Science Center at Fort Worth.

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Journal Digest

Is maternal age an independent risk factor for fetal loss?

Nybo Andersen A-M, Wohlfahrt J, Christens P, Olsen J, Melbye M. Maternal age and fetal loss: population based register linkage study. *BMJ* 2000;320:1708-1712

DESIGN AND SETTING

To study the effects of maternal age on fetal loss, data on reproductive outcomes were obtained from three Danish population-based health registries. Reproductive outcome was defined as live birth, stillbirth, spontaneous abortion, hydatidiform mole, ectopic pregnancy, or induced abortion. The risk of fetal loss according to maternal age was estimated as a proportion of all pregnancies intended to be carried to term—that is, live births, stillbirths, spontaneous abortions (including hydatidiform mole), and ectopic pregnancies. To assess the risk of stillbirth according to maternal age, only pregnancies at risk of becoming a stillbirth (ie, a pregnancy carried to 28 weeks or longer) were taken into consideration, and consequently, the risk constitutes the proportion of stillbirths among all births.

SUBJECTS

All women with a reproductive outcome in Denmark from 1978 to 1992 were included in the study. There were a total of 634,272 women and 1,221,546 pregnancy outcomes.

MAIN OUTCOME MEASURES

The outcomes measured were age-related risk of fetal loss, ectopic pregnancy, and stillbirth and age-related risk of spontaneous abortion stratified according to parity and previous spontaneous abortions.

MAIN RESULTS

Overall, 13.5% of the pregnancies intended to be carried to term ended with fetal loss. The risk of all fetal losses according to maternal age at conception followed a J-shaped curve, with a steep increase after 35 years of age (see figure). More than one fifth of all pregnancies in 35-year-old women resulted in fetal loss; for women at 42 years of age, more than half of the intended pregnancies (54.5%) resulted in fetal loss. The association between maternal age and spontaneous abortion had a curve similar to that for all fetal losses. There was an increased risk of spontaneous abortion in women with increasing maternal age, regardless of parity, number of previous spontaneous abortions, or calendar period (1978-1982, 1983-1987, or 1988-1992). The risk of spontaneous abortion varied from a minimum of 8.7% by the age of 22 years to 84.1% by the age of 48 years or older. While the overall risk of spontaneous abortion increased in the years of the study, calendar period or maternal birth cohort did not confound the association between maternal age and risk of spontaneous abortion. The incidence of ectopic pregnancy showed a steady increase with increasing maternal age. At the age of 21 years, 1.4% of women had ectopic pregnancies, whereas 6.9% of pregnancies in women aged 44 years and older were ectopic. The association between maternal age and stillbirth also showed a J-shaped curve, but the effect was less than for spontaneous abortions and ectopic pregnancies.

CONCLUSIONS

There is an increasing risk of fetal loss with increasing maternal age in women aged more than 30 years. Fetal loss is high in women in their late 30s or older, irrespective of reproductive history. This should be taken into consideration in pregnancy planning and counseling.

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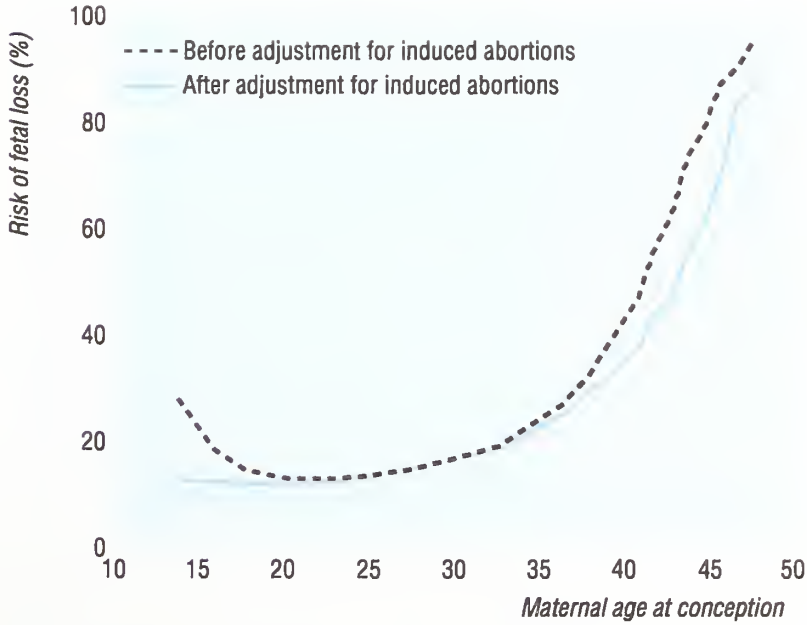

Risk of fetal loss from spontaneous abortion, ectopic pregnancy, and stillbirth according to maternal age at conception (yr)

Does daily use of sunscreen or β-carotene supplements prevent skin cancer in healthy adults?

Green A, Williams G, Neale R, et al. Daily sunscreen application and betacarotene supplementation in prevention of basal-cell and squamous-cell carcinomas of the skin: a randomized controlled trial. *Lancet* 1999;354:723-729.

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DESIGN AND SETTING

Randomized controlled trial, with a 2×2 factorial design and a 4.5-year follow-up, conducted in subtropical Queensland, Australia.

PARTICIPANTS

A total of 1,621 participants (mean age 49 years, 56% of whom were women) who were aged 20 to 69 years when they completed a skin cancer survey in 1986, had completed a second survey in 1992, and had a complete skin examination by a dermatologist with removal of all diagnosed tumors of the skin. Follow-up was 85%.

INTERVENTION

Participants were allocated to 1 of 4 groups: daily use of sun protection factor 15 plus a broad-spectrum sunscreen (to cover exposed sites on head, neck, arms, and hands) and β-carotene, one 30-mg tablet per day (n = 404); daily sunscreen use and placebo tablets (n = 408); β-carotene use alone (n = 416); and placebo alone (n = 393). Participants in the groups receiving β-carotene alone or placebo alone were told they could continue using sunscreen at their usual discretionary rate (74% of these adults used sunscreen ≥2 days per week).

MAIN OUTCOME MEASURES

Person-time–based incidence and total tumor incidence of basal cell carcinoma or squamous cell carcinoma that was diagnosed 1 or more years after the intervention began.

MAIN RESULTS

Basal cell carcinoma developed in 65 adults who used sunscreen daily and 63 adults who did not use sunscreen daily; for squamous cell carcinoma, the respective numbers were 22 and 25. The differences were not statistically significant (basal cell carcinoma rate ratio: 1.03, 95% confidence interval [CI] 0.73-1.46; and squamous cell carcinoma rate ratio: 0.88, CI 0.50-1.56). Among adults who received β-carotene supplements, basal cell carcinoma developed in 102 persons, and squamous cell carcinoma developed in 40, whereas the respective numbers for those who received placebo were 93 and 28. The differences were not statistically significant (basal cell carcinoma rate ratio: 1.04, CI 0.73-1.27; and squamous cell carcinoma rate ratio: 1.35, CI 0.84-2.19). Twenty-two people in sunscreen groups had 28 incident squamous cell tumors, and 25 people in control groups had 46 tumors (tumor rate ratio: 0.61, CI 0.46-0.81). Forty-five adults would need to use sunscreen for 4.5 years to prevent 1 squamous cell tumor. The study design had 80% power to detect a 36% difference for basal cell carcinoma and a 59% difference for squamous cell carcinoma.

CONCLUSIONS

The daily use of β-carotene supplements did not reduce the incidence of skin cancer; the daily use of sunscreen reduced incident squamous cell tumors.

Sunscreen was supplied by Ross Cosmetics of Australia and Woolworths Limited Australia. β-carotene supplements and placebo were supplied by Roche Vitamins and Fine Chemicals, New Jersey.

Commentary

Christopher Del Mar, University of Queensland, Herston, Queensland, Australia

The rapid increase in the incidence of skin cancer has led to greater interest in the primary medical practice role for prevention. In the absence of good data to suggest that secondary prevention—that is, early detection of melanomas or squamous or basal cell carcinomas—is worthwhile,[1] it has been hoped that primary prevention—avoiding sunlight—will prove effective. Previous doubts that the use of sunscreen creams (a popular form of primary prevention) actually prevent skin cancer[2] and the possibility that they might even be harmful make a well-designed intervention trial welcome.

The study by Green and colleagues showed that neither oral β-carotene use nor topical sunscreen cream was harmful in the short term. The lack of evidence of benefit suggests that the use of sunscreen to prevent basal cell cancer and of β-carotene supplements to prevent both basal and squamous cell cancer is not effective. However, 2 of the 4 groups (β-carotene use alone and placebo alone) not assigned to use sunscreen were contaminated; 26% of these patients used sunscreen, a fact that would dilute any real effect and reduce the power of the study. Time may confirm a possible benefit of sunscreen use on basal cell cancer because the authors promise to follow up the cohort.

The evidence for the benefit of sunscreen use for incident squamous cell carcinomas of the magnitude of 40% suggests that we should recommend that patients—even middle-aged people—use sunscreen combined with other forms of sun avoidance in sunny climates.

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Best Practice

TOPICS IN REVIEW

Depression in medical illness

The role of the immune system

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Summary points

- Cytokines are nonantibody proteins released by cells on contact with antigens and that act as intercellular mediators
- During physical illness, the immune system serves as a sensory organ, communicating with the brain through the secretion of cytokines
- An association exists between high cytokine levels and psychological disturbances, particularly depression
- Experimental immune activation can lead to depressed mood and other psychological disturbances
- Antidepressants can be used to prevent or treat illness-associated depression, possibly through their immunomodulatory effects
- Depressive symptoms in physically ill patients may be a result of immune activation and cytokine secretion, rather than a psychological reaction to the distress and incapacitation induced by the illness

INTRODUCTION

Many interactions occur between the immune, neural, and psychological systems. These interactions include communication pathways from the brain to the immune system, particularly the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system, that mediate the influence of psychological variables, such as stress and emotions, on immunity and resistance to disease.[1]

In addition, when the body is confronted by pathogens, the immune system serves as a sensory organ, alerting the brain to the presence of infection-induced immune activation.[2] The communication from the immune system to the brain is mediated by cytokines, which are peptides that orchestrate the immune response with a wide range of other biologic activities. During immune stimulation, cytokines such as interleukins and interferons are produced both in the periphery and in the brain, where they can affect neural, neuroendocrine, and behavioral functions through specific receptors.[2,3]

In addition to physiologic responses, such as fever, and hormonal responses, such as activation of the HPA axis, brain cytokines also produce behavioral changes. A person with a physical illness may show depressed mood, anorexia, weight loss, sleepiness and altered sleep patterns, fatigue and retardation of motor activity, reduced interest in the physical and social environment, and impaired cognitive abilities.[3,4] During an acute infection, these behavioral symptoms, collectively termed "sickness behavior," are considered to be an adaptive response, rather than due to the disease process itself and the fever that accompanies it. However, during chronic infections and other chronic medical conditions associated with intense immune activation, the sickness behavior syndrome can develop into a depressive episode. Illness-associated depression can cause high levels of distress in a sick person and may further complicate the existing physical symptoms and compliance with therapy.

In this review, I present the current knowledge on the role of cytokines in mediating the depressive symptoms that accompany various medical conditions. I also consider the possible use of antidepressant drugs—and their mechanism of action—in the treatment of illness-associated depression.

METHODS

This review is based on a MEDLINE search from 1966 to the present, using the search terms "physical disease," "depression," "cytokines," and "antidepressants," together with my own research and publications in the field.

PHYSICAL DISEASE AND DEPRESSED MOOD

Depression is a common, disturbing concomitant of medical conditions. The reported prevalence of major depressive episodes in physically ill patients varies from 5% to more than 40%. However, because depression is often unrecognized and undertreated in sick patients, the prevalence reported in most studies is probably an underestimate.[5]

The high prevalence of depression in various medical conditions is reflected by the special psychiatric diagnosis of "depression due to a general medical condition."[6] To be diagnosed with this condition, "the clinician should establish the presence of a general medical condition and determine that the depression is etiologically related to the general medical condition through a physiological mechanism."[6(p367)] Several lines of evidence suggest that this mechanism involves the immune system. In other words, the depression associated with various medical conditions is not merely a reaction to the incapacitation, pain, and losses that accompany the physical disease process, but may be directly caused by activation of the immune system.[4,7]

The evidence for illness-associated mood changes and a depressive symptom complex is mainly anecdotal, and few

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Depression may be due to immune activation

studies have examined these symptoms systematically. Experimentally induced viral infections (such as common cold and influenza) and the natural occurrence of upper respiratory tract illness or influenza[8-10] produce depressed mood and other depressive symptoms, as well as various neuropsychological impairments. Similar disturbances have also been reported following chronic infections with herpesvirus, cytomegalovirus, Epstein-Barr virus, gastroenteritis, Borna disease virus, and human immunodeficiency virus.[3]

Many noninfectious conditions are also associated with chronic activation of the immune system and secretion of cytokines (first box). Patients with these diseases have a high incidence of depression.[4,11] Studies have shown that immune dysregulation precedes the development of depression. This suggests that illness-associated depression may be causally related to immune activation, rather than being a psychological reaction to the medical condition per se.

My colleagues and I have recently used a double-blind prospective design to investigate the immediate and prolonged psychological and physiologic effects of a specific viral infection in humans.[12] The subjects were 240 teenaged girls who were vaccinated with live attenuated rubella virus. Based on an analysis of the levels of antibodies to rubella, subjects were divided into 2 groups: an experimental group comprising those who were initially seronegative and were infected following vaccination and a control group comprising those who were already immune to rubella before vaccination. Compared with control subjects, and their own baseline, subjects in the experimental group showed a significant rise in several standard measures of depressed mood, as well as an increased incidence of social and attention problems and delinquent behavior.[12] These effects were particularly evident in girls from low, but not middle or high, socioeconomic status and could be predicted by personality traits measured at baseline.[13] Thus, even a mild viral infection can produce a prolonged increase in depressive symptoms in vulnerable persons.

ROLE OF CYTOKINES IN ILLNESS-ASSOCIATED DEPRESSION

The best evidence for the involvement of cytokines in mediating the psychological effects of physical disease is that the exogenous administration of cytokines in patients with cancer or with hepatitis C produces marked psychological and neuroendocrine symptoms that are similar to those induced by viral infection.

The administration of cytokines (interferon alfa, interleukin [IL] 2, or tumor necrosis factor [TNF]α) causes flulike and depressive symptoms (second box).[14] The fact that these symptoms appear almost immediately after cytokine administration and usually disappear shortly

Noninfectious conditions associated with chronic activation of the immune system and secretion of cytokines

- Autoimmune diseases: multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, and allergy
- Stroke
- Trauma
- Alzheimer disease
- Other neurodegenerative diseases
- Cancer

Depressive symptoms caused by administration of cytokines to patients with cancer or hepatitis C

- Depressed mood
- Dysphoria
- Anhedonia (reduced capacity to experience pleasure)
- Helplessness
- Mild to severe fatigue
- Anorexia and weight loss
- Hypersomnia
- Psychomotor retardation
- Decreased concentration
- Confusion

after termination of the cytokine treatment strongly suggests a causal role for cytokines in producing the depressive symptoms.

To further examine the role of cytokines in the psychological alterations that accompany infection and inflammation, my colleagues and I recently studied the effects of lipopolysaccharide (LPS) on affective and cognitive variables in healthy volunteers.[15] The administration of a low dose of purified LPS (the major cell wall component of gram-negative bacteria) is the most established and frequently used experimental model for safely and accurately assessing the initial host response to infection in humans. We used a crossover design, in which each subject completed a battery of psychological and neuropsychological tests at various times following LPS injection on 1 day and following the administration of saline solution on another day. We used a double-blind design, in which neither the experimenter nor the subject knew the group assignment. LPS had no effect on physical sickness symptoms, blood pressure, or heart rate, but it caused a mild increase in temperature and markedly elevated the circulating levels of many cytokines and cortisol. Following LPS administration, the subjects showed a transient substantial increase in levels of anxiety and depressed mood. In addition, verbal and nonverbal memory functions were substantially impaired.

Significant positive correlations were found between the secretion of specific cytokines (such as IL-6 and TNFα) and LPS-induced depressed mood and anxiety and the severity of memory impairments.[15] The findings suggest that in humans, a mild stimulation of the primary host defense—that does not induce subjective symptoms of physical sickness—is associated with emotional and cognitive disturbances, which may be caused by cytokine release.

Studies in animals provide more direct evidence for the role of cytokines in mediating the behavioral effects of various pathogens. As found in humans, both infectious and noninfectious diseases in animals are associated with anorexia and weight loss; hypersomnia; psychomotor retardation; fatigue; anhedonia; and impaired cognitive abilities, exploration, and social behavior.[2,3,11] Similar sickness behavior symptoms can be observed following the exogenous administration of cytokines (particularly IL-1β and TNFα), either in the periphery or directly into the brain.[4,11,16] Moreover, the behavioral effects of immune challenges can be attenuated by pretreatment with cytokine synthesis blockers and cytokine antagonists, as well as by the manipulation of cytokine genes.[4,11,16]

ANTIDEPRESSANTS REDUCE ILLNESS-ASSOCIATED DEPRESSION

Antidepressant medication has been used successfully in treating depressive symptoms associated with medical illness.[5] Both tricyclic antidepressant medications and selective serotonin-reuptake inhibitors are of proven value in treating depression associated with a wide range of conditions (third box).[17-21]

Conditions associated with depression in which depressive symptoms respond to antidepressants

- Multiple sclerosis
- Stroke
- Alzheimer disease
- Cancer
- Human immunodeficiency virus infection
- Interferon administration (eg, to patients with hepatitis C or multiple sclerosis)

Antidepressants have been shown to have many immunomodulatory effects. In vitro, exposure to antidepressants is mainly immunosuppressive, particularly with respect to cytokine secretion from human immune cells.[22-25] In depressed patients, antidepressants may also have immunomodulatory effects. Studies have shown conflicting results—long-term treatment with antidepressant medication has been associated with the suppression of immune function and cytokine secretion, an increase in cytokine production, or no effect on cytokine levels.[26]

To further elucidate the relationship between immune activation and depression and to explore the mechanisms underlying the therapeutic action of antidepressants, we used an experimental animal model. Specifically, we examined the effects of antidepressants on LPS-induced behavioral and neuroendocrine alterations in rats.[27] We showed that long-term but not initial administration of imipramine or fluoxetine attenuated or completely abolished LPS-induced sickness behavior as well as some of the physiologic and neuroendocrine effects of LPS.[11,27]

In a recent study, this procedure has been adopted for the treatment of cytokine-induced depression in humans. In a double-blind, placebo-controlled design, patients were pretreated with the antidepressant, paroxetine, or placebo for 2 weeks before the initiation of long-term high-dose interferon therapy for malignant melanoma.[28] Most patients receiving placebo met the criteria for major depression or had to discontinue interferon because of toxic reactions before 3 months. In contrast, less than a third of the patients receiving paroxetine developed depression, and no patients taking paroxetine had dropped out of treatment, representing a statistically significant improvement in morbidity and compliance. Together, these data indicate that antidepressants provide useful treatment and prophylaxis against the development of illness-associated mood disorders.

CONCLUSION

Accumulating evidence indicates that immune activation during various medical conditions is associated with a depressive syndrome. Taken together with the reports that brain cytokines influence the neurochemical systems involved in depression,[11] these findings support the hypothesis that immune activation, through the release of cytokines, is involved in the cause and symptoms of illness-associated depression. Antidepressants have effective protective and therapeutic effects on illness- and cytokine-mediated depressive episodes. Future research should examine the effects of cytokine-synthesis blockers and antagonists on mood disorders associated with medical conditions.

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The curriculum template: creating continuing medical education curricula for physicians in practice in managed care settings

INTRODUCTION

As managed care took hold across the United States in the early 1990s, physician leaders acknowledged that doctors were ill prepared for managed care practice.[1,2] Managed care organizations (MCOs) lamented the dearth of physicians trained in managed care principles,[3,4] while academic medical centers acknowledged the need to prepare physicians to practice in the managed care environment.[5] With these needs in mind, we hypothesized that continuing medical education (CME) efforts that taught skills for working in a managed care environment would be well received by physicians in California. Partnerships between academic medical centers and MCOs were already occurring in graduate medical education.[6] Were they not also natural partners for collaborating to provide managed care CME?

This report describes the results of a "joint venture" begun in 1994 between medical teaching institutions and MCOs to develop on-the-job CME for physicians caring for managed care patients.

BACKGROUND

For the majority of US physicians, managed care has represented an historic shift in the definition of their professional work. The individual physician is no longer the principal arbiter of the nature, choice, availability, and costs of health care services. Capitation payment for a defined population, clinical prevention, gate keeping, restricted access to specialists, utilization review, practice profiles, clinical guidelines, and outcomes management are policies that MCOs implement on an individual patient and physician level. Whether salaried employees of an MCO or members of a large medical group that contracts with one, physicians are now subject to these policies that directly affect their daily work-life.

As medical educators in a community hospital setting, we were eager to find CME programs designed to help physicians make the transition to managed care practice. We expected that they would need strategies for addressing the common patient care problems encountered in clinical settings. For example, within a 15-minute visit, how does one elicit an essential database on a 49-year-old obese diabetic patient who presents with new-onset chest pain?

The CME programs we found were disappointing. Although physicians could now attend seminars on how to select billing system software, negotiate a "withhold," or write a practice guideline,[7-9] we found no programs that focused on the actual process of providing care to patients. It was as if caregiving per se—such as listening to patients and diagnosing illness—would continue unchanged under managed care. Was it anticipated that the new managed care policies and the changes they generated could be easily integrated into the daily practice of medicine? On a practical level, we wondered about physicians' ability to reliably meet increasing productivity standards while maintaining quality of care and professional satisfaction. It remained, therefore, to create CME efforts that could meet these challenges.

Additional information about the curriculum template appears on our Web site at www.ewjm.com

Summary points

- There is a lack of continuing medical education to address the daily work of practicing medicine in the managed care setting
- Physician competence for managed care practice requires definition via curricula
- Eighteen California clinicians and educators from managed care organizations and academic medical centers engaged in a process to create a template for developing curricula
- The template focused on physicians "in relationship" with managed care organizations, their patients, and their colleagues, as well as in tandem with their professional and private selves
- The template offered an interdisciplinary, small group venue that allowed protected time for case-based discussion
- Medical educators and managed care leaders can reconstruct managed care organizations to put relationship-based practice firmly in place

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METHODOLOGY FOR DEVELOPING THE CURRICULUM TEMPLATE

We hypothesized that the creation of a CME curriculum relevant to the needs of physicians practicing in managed

care setting could best occur through collaboration between teaching centers and MCOs. To jump-start a working relationship, we sought extramural support from the Pew Commission on Health Education's Center for the Health Professions at the University of California, San Francisco. Through phone calls, letters, and visits, we began by gauging the interest among California medical educators and managed care leaders for the development of a different kind of CME program from those currently available. We proposed that managed care CME focus explicitly on caregiving—those traditional tasks involved in seeing patients, such as taking a history, making referrals, and discussing the prognosis.

Ten California teaching centers and 15 MCOs and medical groups expressed interest in collaborating on CME curricula for managed care. To start, we convened a panel of 18 clinicians and educators to reach consensus on the purpose, content, and methods for the curricula. The panel consisted of 6 practicing physicians (2 in private practice, 4 in managed care settings), a physician in residency training, 2 physician-administrators in MCOs, a nurse, a social worker, a medical ethicist, a consumer representative, and 5 medical educators from a variety of educational settings. Rather than create an actual curriculum, the panel's task was to develop a "template": a document for writing curricula consistent with specified objectives and methods. To create the template, panel members participated in a Delphi process (see box) that employed 4 rounds of mailed questionnaires and summarized anonymous responses iteratively to gain consensus over an 8-month period. The questions probed the nature of doctoring under managed care, the competencies needed for that practice, methods for introducing content arenas, and strategies for curricula evaluation. Short position papers by panel members on content arenas and teaching methods issues were shared. Between the second and third rounds, a one-day conference helped panel members prioritize essential competencies and methods. A finished document, "The Curriculum Template," was completed in 1995 and mailed to the MCOs and teaching centers that had expressed initial interest. They would use the template to develop year-long demonstration efforts in the MCO setting through, figuratively, cordoning off sections of physicians' everyday practice life for on-the-job CME.

The Delphi technique

The Delphi technique is one of several methods for soliciting and using opinions, perceptions, and ideas of others. It asks individuals to provide their opinions or answers to questions anonymously, then while preserving their anonymity, feeds back the answers to the individuals for reflection on their original thoughts. This feedback process can be repeated until significant convergence of opinion is obtained.

Curricular content: relationship arenas

The template was directed at physicians in their daily work of doctoring. Because the basic nature of doctoring is a social one, addressing their daily work meant focusing on physicians "in relationship."[10] The template delineated competencies in 4 relationship areas:

- The relationships (primarily contractual) that physicians have with the MCO
- The relationships physicians have with their patients
- The relationships physicians have with other caregivers
- The internal relationship physicians experience between the private and professional realms

Arena one: relating to the MCO

By contracting with an MCO, the physician becomes its partner in providing the covered care. To the patient, the physician is the MCO's point person for integrity, access, and overall effectiveness as an organization. At least 4 responsibilities relate to this role:

- Acquiring appreciation of the MCO's philosophy regarding care provision
- Learning managed care principles and how they operate
- Understanding conflict resolution process resulting from physicians' roles both as patient fiduciaries and MCO contractors
- Collaborating in MCO policy development

Arena two: negotiating the doctor-patient relationship over time

In the optimal doctor-patient relationship, the physician negotiates between state-of-the-art medicine and the subjective reality of the patient. Today, interjected between the 2 is the patient's MCO. The MCO defines the context in which the physician exercises medicine's core competency—establishing and maintaining a trusting patient-doctor relationship. The relationship is a work-in-progress, requiring ongoing attention to ensure that the patient's illness experience is understood, affirmed, and with mutual consent, opened up for intervention. A growing body of evidence has strongly suggested what many have known intuitively—the positive correlation between an effective patient-doctor relationship and positive patient outcomes.[11-13]

The template panel observed that this "relationship competency" has been eclipsed by the newer managerial and technology-oriented skills that are expected of physicians today. The panel believed the CME curriculum that highlights these skills while neglecting the doctor-patient relationship will, in the end, jeopardize the tremendous potential managed care has for enhancing care quality.

The primacy of this relationship in the managed care setting has only recently gained the attention it deserves.[14]

Arena three: collaborating with others

Collaboration with physician and non-physician colleagues in the provision of direct patient care takes on heightened meaning in managed care. At heart is the belief that the physician should share the work of patient care with those who have the knowledge and skills required by the patient. Working in an interdisciplinary team is an excellent way to appreciate one's limits as a clinician.

Arena four: coping with one's private/professional self—an internal relationship

The template panel believed that to the extent physicians have opportunities to reflect on their work with patients, they would not only avoid burnout, but develop faster as productive, self-aware health care professionals. Self-aware physicians gain insight into their decision-making styles and how the patient, the organizational context, and their own values affect decision making. This is best done through reflecting on one's practice in the company of like-minded peers during time set aside in the work schedule at the work site. As care providers share clinical stories, they become aware of the signs of distress in themselves and can take steps to address them openly.

Curricular methods

Lecture-based CME programs without clear links to the physician's own practice has shown little effect on physician behavior.[15,16] In the 1990s, American and Canadian educators began testing methods that highlighted the practice as the milieu for both assessment and remediation. They stressed learner identification of real as opposed to perceived knowledge gaps revealed through practice audits, interaction with colleagues in small groups using actual cases, and longitudinal sequenced learning experiences.[13,17,18]

The template panel believed that small group methods should be the CME method of choice for delivering curricula content. Because some physicians could be reluctant to join a small group, a short seminar series would introduce the curricula (see box). Fast-paced, didactic sessions on topical subjects would be followed by small group discussions where opinion leader physicians would recruit their peers for subsequent meetings in "colleague groups."

The colleague group

A colleague group would be composed of 6 to 10 health professionals representing a mix of clinician specialties and health disciplines. At minimum, it would include primary care physicians, medical specialists, nurses, social workers, and psychologists. Meeting at least monthly in the office or clinic setting, the physician participants would reexamine core doctoring competencies while simultaneously practicing newer complementary skills (eg, clinical guideline review). Encouraging colleague groups to meet during the workday would be an indication of an MCO's commitment to their caregivers' professional development.

The group's primary task would be to discuss the clinical care given to individual patients. The case presentation would be the basic venue, with at least 2 cases presented at each session. On a predetermined schedule, each group member would be responsible for presenting a particularly challenging case. Through facilitated discussion, participants would become acquainted with methods for reflecting on their practices (see box). Over time, participants would become comfortable in presenting daily practice dilemmas. When faced with recurring clinical topics (eg, early identification of dementia), the group would study its prevalence in their individual practices. Based on their

Sample topics for seminar series

Understanding the MCO

- The struggle between fee-for-service medicine and managed care—impact on clinical decision making
- The 4 Es of managed care: economics, ethics, effectiveness, and efficiency

Negotiating the doctor-patient relationship

- The patient interview: eliciting and addressing the patient's agenda
- Adherence and placebos: the evidence

Collaborating with physician and nonphysician providers

- Real-time collaboration with nurses and social workers
- The truth about teams

Understanding the physician decision maker and the doctoring context

- Stressful clinical decisions
- Learning methods for "reflection in action"

Methods for clinicians to reflect on their practices

- Examining how uncertainty, clinical context, and organizational milieu affect decision making
- Understanding one's practice profile and its implications for decision making (eg, patients' cultural backgrounds)
- Experimenting with different patient and colleague communication styles
- Discussing core beliefs and attitudes about the work of caregiving

findings, they would identify learning gaps and care delivery deficits, search for relevant evidence from the literature, and develop new approaches to test in their practices. If broader educational needs or potential quality of care issues surfaced, they would be referred through appropriate channels of education or continuous quality improvement. Colleague group facilitators would be practicing physicians selected from the MCO or the teaching institution for their role as informal opinion leaders. They would receive training in small group facilitation, clinical decision making, and evidence-based medicine. Their role would be to explicitly connect the material from the small group to the 4 curriculum areas.

OUTCOMES

Seven pairs of MCOs and teaching centers used the template to draft their own curricula. Individual curricula focused on specific population groups (eg, low-income working families) and proposed using small-group, case-based methods. Although not culminating in demonstration projects as originally planned, the efforts stimulated CME within the respective institutions and influenced several managed care educational initiatives at other centers.[19-21]

CONCLUSIONS

The curriculum template offered a sharp contrast in content and methods to the managed care education popular throughout the 1990s.[22-24] As opposed to lectures by corporate-sponsored experts at vacation conference centers, the template called for the creation of small, interdisciplinary clinician groups at the work site. In these groups, theoretical constructs of clinical prevention, continuous quality improvement, and evidence-based medicine would become firmly grounded in the stories of real patients, the responses of actual clinicians, and the relationships that developed between them. As the managed care industry struggles to redefine its product and the public questions whether physicians can be trusted as fiduciaries, the time is ripe for educators and managed care leaders to reconstruct managed care medicine by putting relationship-based practice firmly in place.

The curriculum template panel members were: Steven Freedman MD, Gerrie Gardner DO, Halsted Holman MD, Irving N Klitsner MD, Robert Larsen MD, Steven Lauterbach MD, Suzanne Leib MFCC, Guy Micco MD, Dayton Misfeldt MD, Ellie Prentis RN, Don Ransom PhD, Rachel N Remen MD, Joel Satzman MD, Joseph E Scherger MD MPH, Rosabella Tobriner, Lu Ann Wilkerson PhD, Michael Wilkes MD, and Laurie Zoloth-Dorfman PhD.

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Medicine Cabinet

Migraine prophylaxis in adult patients

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Summary points

- Not all patients are candidates for prophylactic therapy for migraine; physicians must evaluate whether prophylaxis is indicated in a patient
- Prophylaxis of migraines is not a cure; abortive measures will still be necessary in most patients
- A headache diary is essential to identify and avoid triggers and to evaluate therapy
- For prophylactic drug therapy, choose the agent that has the potential for the highest benefit and lowest risk to the patient
- Although their efficacy is questionable, alternative therapies may have some role in migraine prophylaxis

INTRODUCTION

Migraine headaches can be debilitating if patients cannot control or minimize the symptoms, and they can substantially impair the quality of life. However, migraines can often be successfully controlled by the avoidance of triggers, lifestyle changes, and abortive treatment. In patients in whom these measures prove insufficient or unsatisfactory, prophylactic measures to prevent migraines may be needed.[1] A common preventive measure is the use of prophylactic drugs, which will be the focus of this article. I will briefly mention nonpharmacologic or alternative measures.

SEARCH METHODS

The information given here is based on a MEDLINE search from 1966 to the present using the terms "migraine prevention" and "migraine prophylaxis." The search was limited to English-language review articles and studies with human subjects. I also searched the Internet using the key word "migraine" to link to the Web sites of the *Journal of the American Medical Association* Migraine Information Center and the *American Academy of Neurology.*

BEFORE STARTING PROPHYLAXIS

Patients for whom prophylactic therapy is indicated have the following migraine features:

- More than 2 headaches per month, but fewer than 8 (>8 attacks per month usually indicate overuse of abortive therapy)[2]
- Headaches less frequent but more prolonged (>2 days' duration) or severe attacks leading to substantial disability[1,3]
- Migraines are refractory to abortive treatment measures
- Therapies for acute attacks are intolerable, contraindicated, or overused (>2 per week)[2-4]
- Migraines are predictable in occurrence
- The patient has other migraine conditions such as migraine with prolonged aura or hemiplegic migraine[5]

Before prophylaxis is appropriate, the physician must evaluate whether proper and adequate abortive therapies have been instituted. Some patients overuse abortive measures, leading to rebound headaches. In these patients, the drug should be withdrawn before preventive therapy is initiated.[2,6]

A headache diary is essential for all patients who suffer from migraine headaches.[7] If migraine triggers can be identified, prophylactic therapy may be unnecessary. If, however, the triggers are unavoidable or undetermined, drug therapy is indicated to try to prevent the migraines. If prophylactic therapy is initiated, a 2- to 3-month trial is generally needed to assess the efficacy of the regimen.[5] Prophylaxis may be daily on a continuous basis or scheduled according to predetermined triggers, such as the onset of menses. The physician should evaluate previous prophylactic measures, if any, for adequacy and appropriateness. Women of childbearing age should be treated with caution because of the teratogenicity of most prophylactic drugs.[2]

Patients must also understand the goals, limits, and risks of migraine prophylaxis. The goals are to reduce the duration, frequency, and severity of the attacks to improve the patient's quality of life and minimize disability.[5] Prophylactic therapy is rarely curative; therefore, abortive therapies continue to be necessary in most patients, although their effectiveness is usually increased when used with prophylactic drugs.[6] A 50% reduction in the frequency of migraines is generally deemed successful.[8] Compliance is a major issue because patients experience medication side effects before any benefit from prophylactic drugs.[3]

CHOOSING AN AGENT

Many drugs have proven efficacy in preventing migraine. Based on patient-specific indices, the agent with the highest risk-to-benefit ratio should be used. The efficacy, contraindications, precautions, side effects, concurrent disease states of the patient ("special indications"), compliance issues, and cost should all be considered.[1,5,9] Side effects must be given special consideration because migraine sufferers have an increased frequency of adverse effects compared with other patients.[2,3]

Guidelines for migraine prophylaxis

- Initiate the chosen drug at a low dose and titrate up (usually evety 2-4 weeks) until benefits occur or side effects prevent any further increase in dose. Long-acting formulations may improve compliance[2,5]
- A 2- to 3-month trial is needed to assess the efficacy of a regimen
- After 1 year, try to withdraw the drug, even if it has been effective.

- Use a drug that may benefit any comorbid conditions the patient has[5]
- Prophylaxis should be monotherapy whenever possible. Combinations of drugs have not shown substantial benefit except in some patients with multiple comorbid conditions.[2]

DRUGS WITH AN ESTABLISHED ROLE IN MIGRAINE PROPHYLAXIS

First-line agents

The first-line agents with the greatest efficacy are β-blockers, tricyclic antidepressants, and divalproex sodium or valproic acid. I have not considered agents unavailable in the United States, such as flunarizine, lisuride, and pizotifen.[1] I have also excluded agents that have proved to be ineffective or for which proof of efficacy is limited.

β-Blockers

The scientific and clinical evidence supports β-blockers as the drugs of choice for the prevention of migraines.[7] The most commonly used agent is propranolol hydrochloride. Generally, if 1 agent fails, another in its class may be tried, and this change may prove to be effective. It is imperative that abrupt stoppage of therapy is avoided.[2] β-Blockers are not effective in reducing aura.[7] In general, response to these agents is gradual, and it may take at least a month to see an effect.[10] The use of β-blockers with intrinsic sympathomimetic activity (such as pindolol) should be avoided.[11] The daily dose range for β-blockers in migraine prophylaxis, together with their side effects, precautions, and special indications, are given in the first box.[5-7,10]

Tricyclic antidepressants

Tricylic antidepressants are another class of medication considered as first-line treatment in migraine prophylaxis. Even without the presence of depression, these agents are effective in preventing migraines, and the response is usually more rapid (within 4 weeks) than with β-blockers.[10,12,13] Combined use with β-blockers does not reduce the incidence of migraines, but it may reduce that of tension-type headaches.[7] Although the entire class is considered useful in prophylaxis, tertiary amines, such as amitriptyline, are more effective than the secondary amines, such as nortriptyline.[6] Amitriptyline hydrochloride is the first-line agent of choice among the tricyclic antidepressants.[5] Physicians need to consider the differences in side-effect profiles of the various drugs when deciding which one to use (second box).[5-7,10,14]

Divalproex sodium or valproic acid

Divalproex and valproic acid are also first-line agents in migraine prevention, and the former has been approved by the Food and Drug Administration (FDA) for this indication (third box).[5-7] The initial dose is usually from 250 mg daily, titrated up to 1,500 mg.[5,7] If no benefit is seen at low doses, dose escalation is usually not helpful.[15] A serum drug concentration of 50 to 120 mg/L is considered to be in the therapeutic range, but it is unclear whether such monitoring is necessary or, indeed, indicative of efficacy.[10,16,17] Other anticonvulsants either have no efficacy or have not proved effective at this time.[5]

β-Blockers in migraine prophylaxis

Doily dose ronge (the most effective dose or dose ronge is shown in porentheses)

- Propranolol hydrochloride (should be specifically considered as first-line agent)*: 40 to 320 mg (80-240 mg)
- Timolol maleate (should be specifically considered as first-line agent)*: 20 to 30 mg
- Nadolol: 40 to 240 mg
- Metoprolol tartrate: 50 to 300 mg (200 mg)
- Atenolol: 50 to 200 mg (100 mg)

Side effects

- Fatigue
- Bradycardia
- Dizziness
- Depression
- Impotence
- Bronchospasm
- Nausea (adverse effects are less frequent than with the other first-line agents)

Precautions

- Asthma
- Chronic heart failure
- Diabetes mellitus
- Peripheral vascular disease
- Conduction defects or heart block
- Depression
- Raynaud's disease
- Hypotension

Speciol indicotions

- Concurrent hypertension
- Angina
- Post myocardial infarction
- Tremor
- Anxiety or panic attacks (specifically propranolol)

*Approved by the Food and Drug Administration for migraine prevention

Second-line agents

Calcium channel blockers

Calcium channel blockers are effective second-line agents (fourth box).[5-7,10] They are usually slower in onset than

Tricyclic antidepressants in migraine prophylaxis

Daily dose range (the most effective dose range is shown in parentheses)

- Amitriptyline hydrochloride (should be specifically considered as first-line agent): 10 to 300 mg (30-150 mg)
- Doxepin hydrochloride: 10 to 200 mg (50-150 mg)
- Imipramine hydrochloride: 10 to 200 mg (50-150 mg)
- Nortriptyline hydrochloride: 10 to 150 mg (50-150 mg)
- Protriptyline hydrochloride: 15 to 40 mg

Side effects

- Anticholinergic effects (dry mouth, constipation, blurred vision)
- Sedation
- Postural hypotension
- Agitation
- Tremor
- Seizures
- Sexual dysfunction
- Weight gain

Precautions

- Arrhythmias or cardiac conduction defects
- Urinary retention
- Angle closure glaucoma
- Seizures
- Obesity
- Pregnancy
- Concurrent monoamine oxidase inhibitor use

Special indications

- Tension-type headaches
- Concurrent depression, insomnia, and chronic pain

β-blockers, and an initial increase in headache frequency may occur on starting therapy. They are a viable alternative in patients who cannot tolerate β-blockers.[6]

Nonsteroidal anti-inflammatory drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) can be used daily or intermittently. When migraine triggers are identified or are predictable—such as menstruation—intermittent therapy may be used (using NSAIDs 1 week before menses and then throughout menstruation).[19-21] Naproxen sodium is the most commonly used NSAID for migraine prophylaxis (fifth box),[5-7,10] and the dose is 1,100 mg daily. Other NSAIDs that may be substituted for naproxen are mefenamic acid, flurbiprofen sodium, fenoprofen calcium, ketoprofen, and aspirin.[5] Adverse effects tend to be infrequent with short-term therapy but increase with extended treatment.[3,5]

Michael W. Davidson/The Florida State University

Nifedipine, shown in this photomicrograph, is a viable alternative for patients who cannot tolerate β-blockers

Third-line agents

Two medications that have proved effective in prophylaxis but are reserved for severe or refractory cases are methysergide and phenelzine sulfate. Both should be reserved for use only by specialists in headache treatment.[2,7]

Methysergide is the fourth agent indicated and approved for migraine prophylaxis by the FDA. Because of its side-effects profile, numerous precautions, and contraindications, it has become a last-line drug. Longer than 6

Divalproex sodium and valproic acid in migraine prophylaxis

Side effects

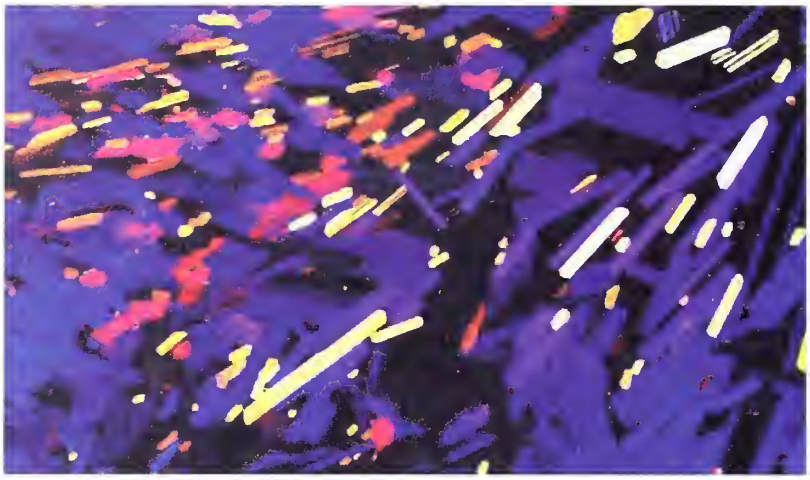
- Nausea
- Vomiting
- Tremor
- Weight gain
- Hair loss
- Drowsiness
- Ataxia
- Hepatotoxicity

Precautions

- Liver disease
- Thrombocytopenia
- Pregnancy
- Young children (high risk of hepatotoxicity)

Special indications

- Prolonged or atypical migraine aura
- Tension-type headache
- Concurrent epilepsy, mania, trigeminal neuralgia, cluster headache



Michael W Davidson/The Florida State University

Nonsteroidal anti-inflammatory drugs, such as aspirin (shown in this photomicrograph), can be taken to prevent migraine

months of continuous use can lead to fatal retropleural, retroperitoneal, or cardiac fibrosis, and drug holidays must be instituted when methysergide is used.[3,7]

Phenelzine—a monoamine oxidase inhibitor—has numerous precautions and contraindications. It should be considered only in severe refractory cases, specifically those that are compounded by tension headaches or atypical depression,[7,22] and only in patients whose compliance can be expected. Phenelzine is difficult to use—it has several potentially dangerous interactions with other drugs, and it can cause hypertensive crises in patients who do not comply with a tyramine-free diet.[6,7]

Calcium channel blockers in migraine prophylaxis

Daily dose range (most effective dose shown in parentheses)

- Verapamil hydrochloride: 120 to 480 mg (240 mg)
- Nifedipine: 30 to 90 mg
- Diltiazem: 120 to 360 mg
- Nimodipine: 60 to 120 mg

Side effects

- Constipation (especially verapamil)
- Dizziness
- Hypotension
- Peripheral edema
- Weight gain

Precautions

- Ventricular dysfunction
- Heart block
- Hypotension
- Bradycardia
- Sick sinus syndrome
- Pregnancy

Special indications

- Prolonged or atypical aura[18]
- Concurrent angina, hypertension, and arrhythmias

NSAIDs in migraine prophylaxis

Side effects

- Dyspepsia
- Erosive gastritis
- Peptic ulceration
- Occult gastrointestinal bleeding
- Hematologic complications

Precautions

- Hypersensitivity to aspirin or other NSAIDs
- Active gastrointestinal bleeding
- Peptic ulcer
- Liver disease
- Kidney disease
- Elderly patients
- Coagulopathies

Special indications

- Concurrent arthritis, dysmenorrhea, and stroke (specifically with aspirin)

DRUGS WITH AN UNCERTAIN OR UNPROVEN ROLE IN MIGRAINE PROPHYLAXIS

The efficacy of fluoxetine hydrochloride has not been well established in prophylaxis, but some experts already consider it a viable alternative to tricyclic antidepressants.[5-7,14] Doses from 20 mg every other day to 40 mg a day have been used. Other selective serotonin-reuptake inhibitors may prove to be useful, but the evidence for their efficacy is so far weak or nonexistent.[5]

Some evidence exists that riboflavin (vitamin B_2) in high doses (400 mg daily) has some effect in migraine prophylaxis. Because of its low cost and low side-effect profile, it may prove to be a useful alternative.[23] Similarly, magnesium at doses of 400 to 600 mg daily may also be of benefit, but there is less evidence for its efficacy than that for riboflavin.[5,24,25]

NONPHARMACOLOGIC MEASURES IN PREVENTING MIGRAINE

The standard nonpharmacologic approach is the avoidance of triggers to migraines. Avoidance may lower headache frequency by 50%.[26] The following are common migraine triggers:

- Environmental or hormonal factors—noise, odors, hunger or thirst, menses, menopause
- Behavioral changes—stress, sleep deprivation, excessive sleep
- Medications—oral contraceptives, hormone replacement therapy, histamine-2 blockers
- Foods or drinks—cheese, wine, alcohol, chocolate, caffeine[27-29]

POSSIBLE ALTERNATIVE THERAPIES FOR MIGRAINE PREVENTION

Feverfew, an herbal medication (*Chrysanthemum parthenium*), is marketed as being useful in migraine prevention, at a daily dose of 125 mg. Most data support the notion that feverfew is superior to placebo. However, a systematic review failed to substantiate its efficacy.[30] Adverse effects are mild—usually gastrointestinal upset—but withdrawal may lead to increased frequency of headache, anxiety, and sleep disturbances. Its use should be avoided in pregnancy.[31]

Other alternative therapies are used by patients in migraine prevention:

- Relaxation therapy—breathing exercises and muscle relaxation
- Cognitive-behavioral therapy—identification and avoidance of behaviors or responses to migraines that may exacerbate a migraine attack
- Biofeedback techniques—these rely on the premise that patients may be able to control physiologic responses of the body, such as to migraine attacks[6]
- Homeopathy (no better than placebo in most studies)[32]
- Acupuncture
- Reflexology
- Massage
- Temperature changes (hot or cold packs)[29]

There is little evidence of the effectiveness of these therapies. However, because most do not cause any apparent harm, some patients may benefit from these options in treatment when used alone or as an adjunct to prophylactic medications.[6]

Special thanks to Kevin Landa, PharmD, for his assistance with this article. **Author:** Dr Parsekyan received his Doctor of Pharmacy degree from the University of Southern California, Los Angeles, and is a pharmacist in Los Angeles.

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Curbside Consult

Should patients on insulin inform the vehicle licensing authorities?

Greg Nelson/AP

This man experienced insulin-induced hypoglycemia while driving. The police thought he was a drunken driver, and used dogs and physical force to subdue him.

Underlying this question of whether to inform licensing authorities is the deep unrest felt by physicians, patients who have experienced hypoglycemia, and if they have given it some thought, society in general regarding the true safety of the driver taking hypoglycemic agents.

An American Diabetes Association position statement includes "employment/licensure" in its title but does not mention licensure in its text.[1]

What is known about this topic? Cox and colleagues studied 37 type 1 diabetic subjects with a history of severe hypoglycemia by using a sophisticated driving simulator during the gradual induction of hypoglycemia.[2] The subjects were instructed to treat their low blood glucose levels (<72 mg/dL or 4 mmol/L), and to take corrective action if they felt that their driving was impaired. In this study, even mild hypoglycemia led to impaired driving. But only 30% of subjects took corrective action, such as pulling off the road or eating a high carbohydrate snack. The authors concluded that there appears to be no connection between awareness of driving impairment and corrective action.

The Diabetes Control and Complications Trial (DCCT), which showed a 50% to 75% reduction in microvascular end points (eg, diabetic retinopathy) in the intensive treatment arm, also highlighted the risks and limitations of current therapy, namely hypoglycemia.[3,4] Hypoglycemia is the limiting factor in the pharmacologic treatment of diabetes mellitus.[5]

DCCT patients receiving intensive therapy were over 3 times more likely to develop severe hypoglycemia.[4] This translates into episodes requiring assistance from others in 25% of intensively treated patients per year compared to 10% on conventional therapy. Furthermore, those on intensive treatment averaged 2 mild, self-treated hypoglycemia episodes per week compared to 1 per week on conventional treatment. Many type 1 diabetics who have the disease for up to 10 to 15 years develop hypoglycemia unawareness—that is, they may lapse into coma or have a seizure with no premonitory symptoms. Hypoglycemia awareness is related to loss of counter-regulation by glucagon and epinephrine. In patients without autonomic neuropathy, repeated hypoglycemia during attempts to achieve normoglycemia may be the most common cause of such unawareness. As Cryer has noted, this may be reversed by as little as 2 to 3 weeks of meticulous blood glucose control with scrupulous avoidance of hypoglycemia.[5]

All of the sulfonylureas and repaglinide can cause hypoglycemia. Fortunately, thiazolidinediones, metformin, α glucosidase inhibitors, and diet alone do not.

What can be done? Cox and colleagues note that blood glucose awareness training increases awareness of blood glucose fluctuations, results in fewer and less extreme hypoglycemic events, and leads to fewer vehicular crashes when compared to subjects in control groups without such training.[2] Diabetic patients who drive should be encouraged to treat themselves immediately whenever they think that their blood glucose is low or their driving is impaired. We should remember, however, that 45% of subjects in Cox and colleagues' study were willing to drive when their blood glucose was <50 mg/dL (2.8 mmol/L), while 43% of significantly impaired drivers never took corrective action. Loss of judgment may be a cardinal sign of hypoglycemia.

It is prudent for a person with diabetes taking insulin, sulfonylureas, or repaglinide to check their blood sugar level before driving and if it is in or below the 72-90 mg/dL (4-5 mmol/l) range, not to start driving until they have normalized their blood sugar level. All diabetic drivers taking these agents should have a readily absorbable source of sugar available—but those also using an α glucosidase inhibitor may have slower absorption of sucrose (table sugar) and should use pure glucose tablets. It also makes sense to periodically test blood glucose levels on long drives. If available, blood glucose awareness training may reduce the risk of hypoglycemia as a cause of accidents and "near misses." Education of family and friends regarding recognition of hypoglycemia and its treatment is useful. To paraphrase a well-known advertisement, "Friends don't let friends drive hypoglycemic."

If only insulin use was reportable to licensing authorities, there would be enormous resistance and reluctance on the part of diabetic drivers to take insulin, even when needed, and on the part of physicians to prescribe this hypoglycemic agent. Therefore, since it is unclear what licensing agencies would or could do with the information, there appears to be nothing to gain and much to lose with mandatory notification. It would be better to disseminate the guiding principles alluded to in this commentary.

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Culture and Medicine

Physicians and rural America

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PROVIDER SHORTAGES IN RURAL AMERICA

Many rural Americans have limited access to health care. This problem stems from 2 characteristics of the health care system: the many Americans without health care insurance and the tendency of health care professionals to locate and practice in relatively affluent urban and suburban areas.

The relative shortage of physicians in rural areas of the United States is 1 of the few constants in any description of the US medical care system. About 20% of the US population—more than 50 million people—live in rural areas, but only 9% of the nation's physicians practice in rural communities.[1]

Crude comparisons of the physician-to-population ratio in rural versus urban areas can be extremely misleading and provide almost no information about whether shortages or surpluses exist in either location.[2] In 1995—the latest year for which data are available—gaps existed between the supply of active physicians in counties of different size (figure 1). As can be seen in this figure, major differences persist between the aggregate supply in urban and rural areas, with the larger counties having many more physicians per 100,000 population.

But this information obscures the fact that the physician supply has grown in rural areas in the past 20 years, although the growth has not been uniform. The supply of rural physicians has increased modestly in the past few decades, with most of the increase in the larger rural communities adjacent to metropolitan areas (figure 2). Rural supply lags far behind the current urban supply of physicians, but the urban supply of physicians is, in the opinion of many, excessive.

Physician supply in rural areas is closely tied to the specialty mix of American physicians. Specialty has a powerful effect on physician location choice for each of the major specialty groups (figure 3). Family physicians distribute themselves in proportion to the population in both rural and urban locations and are the largest single source of physicians in rural areas. All other specialties are much more likely to settle in urban areas.

Given the expansion of the rural physician supply, it is important to distinguish between rural areas that have definite shortages of critical health professionals and those that have fewer health professionals relative to oversupplied urban areas. Historically, the government has designated areas as seriously underserved based on the physician-to-population ratio within a specific health service area. Populations with too few physicians have been categorized as health professional shortage areas, thus becoming eligible for a broad array of governmental assistance.

Summary points

- There is a relative shortage of physicians in rural areas of America
- The more highly specialized the physician, the less likely he or she will settle in a rural area
- The preference of women for urban practice may pose a problem for the future recruitment of rural physicians
- Although managed care systems can recruit physicians to rural areas, systems are growing slowly in rural areas and their doctors may be of little use to the working poor who have neither Medicaid nor conventional health insurance
- Possible solutions to the problem of physician shortages in rural areas include changing the medical education system so that it trains more physicians who choose rural practice, changing the reimbursement strategies of Medicare and Medicaid, and changing the existing federal and state programs

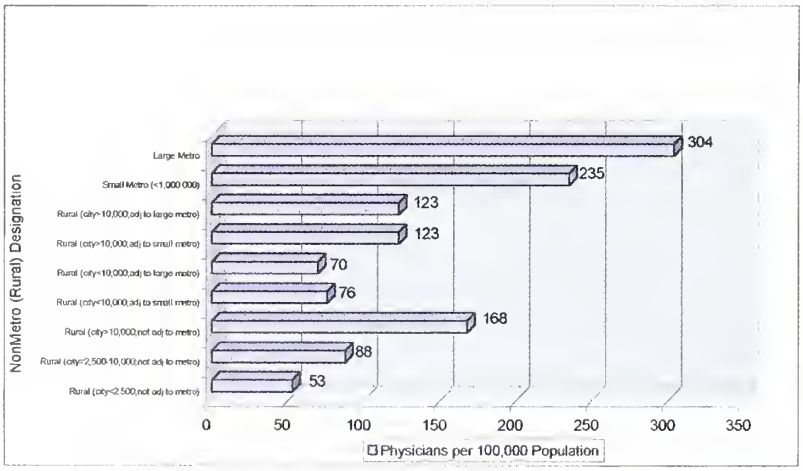

Figure 1 Active physicians per 100,000 population by location, 1995. From AMA from BHPr ARF data, 1997.

Douglas Dickema

Douglas Diekema

EFFECT OF SPECIALTY CHOICE AND DISTRIBUTION

Nothing affects the location decision of physicians more than specialty. The more highly specialized the physician, the less likely he or she will settle in a rural area. As a consequence, the growth of specialization is a major contributor to the geographic maldistribution of physicians. Many of the shortages in communities with fewer than 10,000 residents could have been reduced or eliminated if even a small fraction of subspecialists produced over the past 15 years had chosen to become primary care physicians in rural or underserved areas (T R Konrad: "Shortages of Physicians and Other Health Professionals in Rural Areas: Background Paper Produced for COGME"; Cecil G Sheps Center for Health Services Research, University of North Carolina at Chapel Hill, unpublished, 1997).

The recently revived interest in family medicine and the other generalist disciplines is a major factor in addressing rural geographic maldistribution. The decreasing proportion of generalist physicians leveled off in the 1980s (figure 4).[3] Despite recently increased interest in primary care, the percentage in generalist disciplines has not yet shown a substantial increase. An improvement in the balance of generalists and specialists is a necessary precondition for eliminating rural physician shortages.

EFFECT OF GENDER ON CHOICE OF PRACTICE LOCATION

Starting a decade ago, the proportion of women attending medical school increased rapidly. The number of female physicians in the United States more than quadrupled between 1970 and 1991 and has continued to rise.[4]

Historically, rural medical care was almost exclusively provided by male physicians. This was a product of the paucity of women in medicine and the tendency of the few female graduates to locate in urban areas. Male generalist physicians far outnumber their female counterparts in rural areas across the United States. As the proportion of women in medical schools has increased, there have been concerns that the supply of rural physicians might dwindle if women continue to settle almost exclusively in urban areas and the largest rural cities.

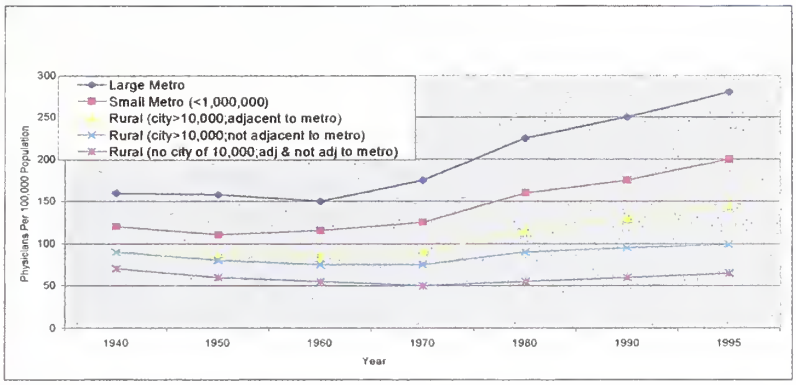

Figure 2 Active physicians per 100,000 population by year and location, 1940 through 1995. From AMA from BHPr ARF data, 1997.

Recent work suggests that the disparity between male and female physicians may be growing less acute with time.[5] The gap between male and female family physicians has narrowed dramatically for more recent graduates (figure 5). Still, even women in the most recent graduate cohort are much less likely than their male counterparts to locate in rural areas, and the disparity is greatest for the smaller and more remote communities. The continuing preference of women for urban practice—even though less pronounced than in earlier years—may still pose a problem for the future recruitment of rural physicians.

INFLUENCE OF MANAGED CARE

Managed care is a major emerging influence on the delivery of rural health care. Although it has become dominant in many urban areas, its effect in rural areas is just beginning to be felt. More than 80% of all rural counties were in the service area of at least 1 health maintenance organization (HMO) by the end of 1995, although the percentage of the rural population enrolled in HMOs is estimated to be less than 8%.[6] Managed care is not only a creature of the private sector; nationally, about a tenth of rural Medicaid

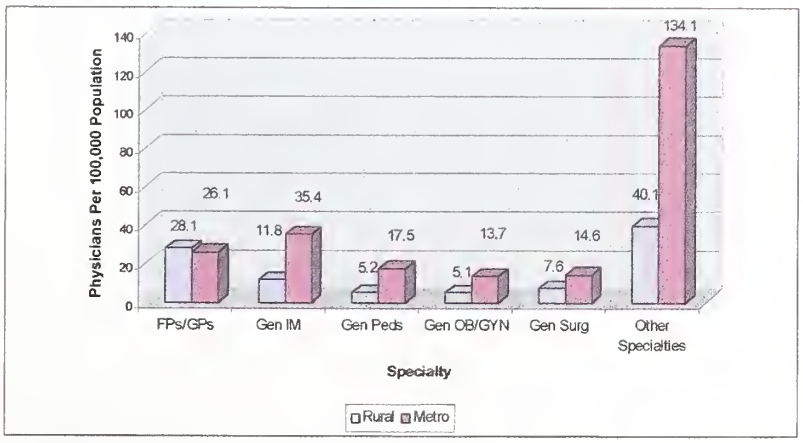

Figure 3 Patient care physicians per 100,000 population by location and specialty, 1995. From AMA from BHPr ARF data, 1997.

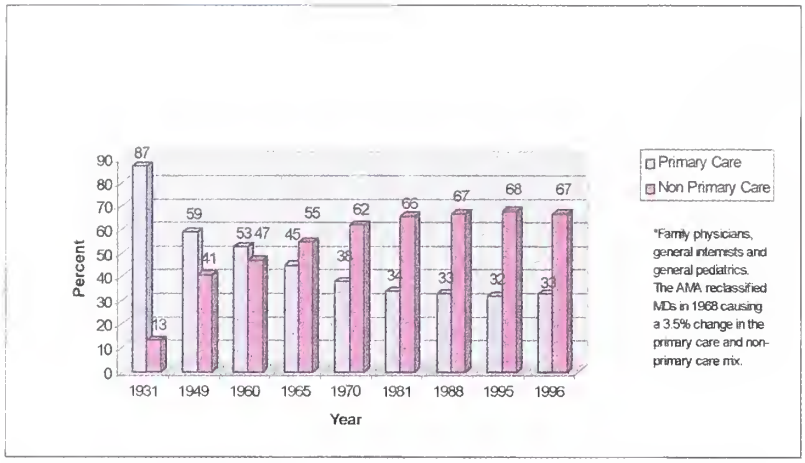

Figure 4 Percentage of primary care and non-primary care physicians for selected years, 1931 through 1996. From AMA from BHPr ARF data, 1997.

recipients are enrolled in Medicaid HMOs and prepaid plans, and the number is increasing rapidly.

Managed care is a 2-edged sword, both with regard to geographic maldistribution and rural medical underservice. Managed care networks have the potential to provide organizational vehicles for hiring and deploying physicians in areas that could not support independent physicians on their own.

But there are 2 potentially adverse effects of managed care systems on rural health: the loss of local control of health care systems and the reluctance of private managed care systems to provide care to the uninsured. Most managed care systems are sponsored by large metropolitan organizations, and these entities may have little understanding of or empathy for isolated rural areas. The presence of physicians hired through vertically integrated systems may mean that the community has health professionals, but they may be of little use to the working poor who have neither Medicaid nor conventional health insurance. The managed care industry is in rapid flux, and the extent to which managed care will ultimately dominate rural areas as it has dominated some urban ones is difficult to predict.

Figure 5 Male to female family or general physicians by graduation cohort, 1997. From Ellsbury KE, Doescher MP, Hart LG. US medical schools and the rural family physician gender gap. *Fam Med* 2000;32:331-337.

POSSIBLE SOLUTIONS TO THE PROBLEM OF INEQUITIES IN RURAL HEALTH

Educational initiatives

One of the most powerful ways to remedy problems of rural geographic maldistribution is to change the medical education system so that it selects, trains, and deploys more health care workers who choose to practice in rural areas. Much of the federal support incorporated within the Title VII programs—the major federal vehicle for generalist training—is based on the premise that this is an achievable goal. Talley has discussed the 4 basic "truths" about rural health[3]:

- Students with rural origins are more likely to train in primary care and return to rural areas,
- Residents trained in rural areas are more likely to choose to practice in rural areas,
- Family medicine is the key discipline of rural health care, and
- Residents practice close to where they train.

To the extent that these relationships are accurate—and evidence supports associations between these characteristics and the decision to practice in rural areas—modifications of the training milieu to incorporate these factors make sense.

The advantage of this approach is that it takes optimum advantage of free-market solutions to the problem of geographic physician maldistribution. Rather than requiring the establishment of federal or state delivery systems that may be controversial, complex, and expensive, graduating residents gravitate to underserved areas to fill their personal desires.

Although this type of intervention does not lend itself to controlled experiments, ample evidence exists that such an approach works. Publicly owned medical schools in rural states, particularly those that see their mission as training future family physicians, have high proportions of their graduating classes ultimately practicing in rural areas. By contrast, research-intensive private schools in metropolitan areas with no commitment to family medicine have virtually no rural graduates.[4]

Changes in reimbursement strategies of Medicare and Medicaid

A powerful mechanism to improve the flow of health professionals to rural areas is the use of targeted incentives. Central to this approach is the belief that physicians and others act as rational economic beings. If some form of economic inducement enhances the reimbursement for rural services, then physicians are more likely to locate in these areas. This approach has been used with some success in Britain, Canada, and Australia, where a variety of bonuses increase reimbursement for selected rural practitioners.

Changes in existing direct federal and state programs

When educational interventions and economic incentives fail to remedy geographic maldistribution, the major recourse is the creation of programs that provide direct services to underserved areas. There are numerous examples of such programs, the largest of which are the community health centers and the National Health Service Corps (NHSC). There is no question that these 2 federal programs remain the preeminent safety net programs for rural America. Studies by the Rural Health Research Centers in Chapel Hill, NC, and Seattle demonstrate that about 1 in 4 of every new primary care physician entering a health professional shortage area in the late 1980s was placed there under NHSC auspices[7] and that 1 in 5 physicians practicing independently in many of the smallest rural communities was initially brought to those areas through their service in the NHSC.[8]

Given the realities of the current system, future efforts should concentrate on improving the fit between need and services, enhanced coordination—and reduced duplication—of services provided, better identification of students to ultimately serve in the NHSC and state programs, and improved effectiveness and efficiency of governmentally sponsored health care services, including those of rural health clinics.[9] The wide variety of programs available—and the natural variability in the way they are organized and administered—leads to enormous complexity in the provision of services. It is certainly worth the effort to simplify programs and their administration and to ensure that governmental resources follow human need, not the administrative prowess of officials who excel at the bureaucratic skills that can obtain these services for their communities.

New technologies: possible effect of telemedicine

Telemedicine is an emerging technology with enormous potential for mitigating the effects of the geographic maldistribution of health professionals. Although telemedicine has a legitimate, important, and growing role in rural medicine,[10] the path to the future is uncertain. As pointed out in the 2nd Invitational Consensus Conference on Telemedicine and the National Information Infrastructure, multiple and significant obstacles exist that make the current efforts uncoordinated, expensive, inaccessible, and at times even illegal.[11]

The current state of telemedicine could be characterized as creative but relatively unstructured, with a wide variety of public and private sector experiments proceeding simultaneously. Some applications, such as reading electrocardiograms at a distance, have become commonplace. Others, such as dermatology consultations, are being performed in many different places but without standard protocols for transmission, interaction, evaluation, or charging. And others, such as doing an appendectomy at a distance, remain in the realm of science fiction, if just barely. From the standpoint of geographic maldistribution, there are 3 key issues (see box).

Key factors in improving the delivery of telemedicine to rural areas

- Resolution of the professional licensure regulations, allowing physicians in metropolitan areas to make their expertise available to remote rural areas, even across state lines
- Clear protocols for a unified technologic infrastructure to reduce costs and to allow rural providers to have the option of communicating with multiple providers of these distant services without being captives of any single information provider
- Reasonable reimbursement by third-party payers for providing medical services at a distance

CONCLUSIONS

Geographic maldistribution of health providers is 1 of the most deep-seated characteristics of the American health care system. Even though the 1990s have been marked by rapid expansion in the absolute and relative number of practicing physicians, substantial rural shortages have persisted. Rural areas will continue to have structural barriers that will require special programs to assist in the training, deployment, and support of health professionals.

This article is adapted, with permission, from Ricketts III TC: *Rural Health in the United States.* New York: Oxford University Press; 1999.

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The Muslim family: predicament and promise

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INTRODUCTION

We live in an era in which the nature, function, and structure of the family have been thrown into question. Many, for example, would consider an unmarried couple, a single mother, and homosexual couples as equally legitimate expressions of the family unit. Islam takes a more conservative stance, arguing that the family is a divinely inspired institution, with marriage at its core. In this article, we explore what the family means for Muslims living in minority communities in the West. Our aim is not to be prescriptive, but rather to provide clinicians with key insights needed to allow their Muslim patients' concerns to be adequately heard.

FAMILY LIFE

One of the most striking features of Muslim society is the importance attached to the family. The family unit is regarded as the cornerstone of a healthy and balanced society.[1] The different plane of emphasis from that found in individual-centered cultures is for many remarkable.

Muslim families: nuclear or extended?

The traditional Muslim family is extended, often spanning 3 or more generations.[2] An extended structure offers many advantages, including stability, coherence, and physical and psychological support, particularly in times of need.

In Muslim culture, akin to other traditional cultures, respect and esteem increase with age. Elderly parents are respected on account of their life experiences and their hierarchic position within the family unit. The opportunity to attend to the needs of one's parents in their later years is viewed as a gift from Allah.

Challenges to the extended family

In practice, it is usual for a new bride to move into the household of her husband. The change is often considerable, and problems in the fledgling relationship between the bride and her in-laws are common. This transition is all the more difficult where Muslims live as minorities because in many cases, migration patterns have resulted in fragmentation of the extended family structure. Many second-generation Muslim migrants have grown up in nuclear families, not having first-hand familiarity with the richness and complexity of living within extended family networks. In addition, despite religious teachings that encourage marriage at an early age, a secular trend to marry late is being seen among Muslims. Some observers have suggested that increasing age curtails a person's ability to adapt to change, adaptability being the hallmark of youth. Finally, and perhaps most important of all, Muslim youth in the West are faced with lifestyle choices not available in more traditional cultures. To some, the opportunities with respect to individual freedom offered by a nuclear family structure far outweigh any benefits of living in an extended family.[2]

Summary points

- The family forms the basic building block of Muslim society. Despite the many pressures it faces, the family institution remains strong. The future of the extended family, however, is under considerable threat
- Female genital mutilation is common among Muslim and non-Muslim women of African origin
- Marriage forms the sole basis for sexual relations and parenthood
- Islamic law generally discourages the use of contraception, extolling the virtues of large families, but there seems to be a trend toward smaller families
- Some social problems such as sexually transmitted infections, cervical cancer, and unwanted pregnancies may be mitigated by developing vehicles to strengthen the traditional Muslim family structure

GENDER AND SEGREGATION

Gender issues and, in particular, the rights of women in Muslim culture, continue to generate much media attention in the West. Muslim women are often portrayed as inferior beings, desperately in need of liberation from the Muslim patriarchal culture that prevents their progress. Segregation of the sexes, a practice encouraged by Islam, is often seen as proof of the suppression of Muslim women.[3] Although certainly much can be done to improve the position of women in Muslim culture, the stereotype created in the western media leaves much to be desired. Such misunderstandings are largely due to naive and simplistic attempts to transpose a western set of norms and values onto women with a very different history and culture. A detailed critique of the feminist position is beyond the scope of this article; readers are referred to other texts.[4,5]

As already noted, Islam clearly demarcates between legitimate and illegitimate human relationships. Societal laws exist to aid Muslims in abiding by this framework. Segregation, therefore, exists primarily to minimize the

chances of illicit relationships developing. Physical contact between members of the opposite sex is strongly discouraged, although these rules are relaxed somewhat if medical treatment is required.[6] This framework explains why many prefer to see a same-sex clinician, particularly in consultations necessitating examination of the genitalia. On a practical note, if recourse to an interpreter is required, the use of same-sex interpreters offers a considerable advantage. The issue of gender segregation is one that should also be considered when planning health education campaigns, research interviews, and similar ventures.

Gender and role demarcation

The man is considered the head of the family; to many a man, however, this is a poisoned chalice because with leadership comes responsibility. Economic responsibility for maintaining the family falls squarely on the shoulders of the man, irrespective of whether his wife is earning money. Unemployment, then, can greatly affect the integrity of the family, leaving the man in a role limbo. Psychological morbidity in such situations may be high, with ramifications for the family as a whole.

MARRIAGE

> You are a garment to them, and they are a garment for you.
>
> Qur'an[7]

This succinct Qur'anic simile encapsulates the primary aims of marriage—to provide warmth, comfort, and protection and to beautify. Within the Islamic vision, children have a right to be conceived and reared in a stable and secure environment; marriage is deemed to provide such an environment. In contrast, celibacy and sex outside of marriage are strongly discouraged because they are considered behavioral extremes that are not conducive to a wholesome society.[8]

In many senses, marriage is considered the union of 2 families, and the parents usually arrange the marriage. Although the free consent of both the bride and groom are essential, parental coercion is often strong.

Some parents are evidently beginning to understand the marital concerns of their children. The practice of choosing marriage partners from within one's community, however, continues to be considered important by young and old.

Consanguinity

Consanguinity (intermarriage) is particularly common in Muslims of south Asian and Arab origin. Among Pakistani Muslims, current estimates are that some 75% of couples are in a consanguineous relationship, and approximately 50% are married to first cousins. This represents an increase from the generation of their parents, of whom only 30% are married to first cousins.[9] Consanguinity confers many advantages, which, at least in part, explain its continued appeal. For example, it allows a thorough knowledge of the future marriage partner for sons or daughters—a particularly important consideration in Muslim minority communities where the usual social networks that facilitate the search for an appropriate partner may be lacking.

Whereas consanguinity doubtless results in an increased frequency of familial disorders with an autosomal recessive pattern of inheritance,[10] assessing the relative contribution of consanguinity to the high rates of congenital defect and perinatal mortality among Pakistanis is far from easy. Other factors of importance in the birth outcome debate include the high prevalence of deprivation among Muslims, difficulties with access to high-quality genetic and prenatal counseling, and the possible risks associated with culturally insensitive maternity care.[11] Appropriate services specifically tailored to meet the needs of Muslims and other minority groups should be considered an issue deserving priority attention.

SEX AND CONTRACEPTION

Sexual norms

Sex in the context of marriage is a legitimate, enjoyable activity—an act of worship that is deserving of Allah's reward. Conversely, sex outside of heterosexual marriage is considered deviant, deserving of punishment in the hereafter.[1] In keeping with orthodox Judeo-Christian teaching, homosexuality is considered sinful. A distinction is made, however, between a homosexual inclination and the act itself. The former is acceptable so long as it is not practiced.[12]

Promiscuity does exist among Muslims, although in all probability its prevalence is considerably lower than in some segments of western society.[13] Those who operate outside the Muslim framework often find themselves ostracized and held responsible for bringing the family name into disrepute. The prospect of "coming out" for homosexual Muslims is, therefore, not realistic at present.

Despite the positive outlook toward sex, it is not a subject that is openly discussed. Cultural taboos dictate that sex should remain a private matter between husband and wife.[8] This explains, at least in part, why Muslims are reluctant to seek help for sexual problems and the long time lag before seeing a physician.

MENSTRUATION

While menstruating, women are exempt from some of the important religious rites, such as ritual prayer, fasting, and

Chris Stowers/Panos Pictures

An extended Muslim family at JFK airport

Hajj (the pilgrimage to Mecca). Sexual intercourse is also prohibited at such times. All other forms of physical contact between husband and wife, for example, hugging and kissing, are allowed. Menstruation, therefore, may have many social and psychological ramifications. There are also many possible implications for clinical care. Women may be reluctant to see a physician for gynecologic symptoms, cervical smear tests, or intrauterine device checks for fear of bleeding following a pelvic examination. Many Muslim women are unaware that traumatic bleeding of this kind is distinct from menstrual bleeding, and hence, the religious constraints do not apply. Education is needed both within the Muslim community and among professionals so that the importance and implications of genital tract bleeding are better appreciated.

Women may consult their physician or family planning clinic to postpone their menstrual periods at particular times. The most common situation is in the period before Hajj. For those using the combined oral contraceptive pill, they can be safely advised to either "bicycle" or "tricycle" pill packs. This involves omitting the 7-day break between pill packs, thus avoiding the withdrawal bleeding that ensues.[14(p53)] Alternatively, progesterone (for example, norethisterone [norethindrone]) may be used daily, beginning 2 to 3 days before the period is due and continuing treatment until such time that bleeding is more convenient.

Additional dimensions in the management of genital tract bleeding

A married woman in her late 30s contacted a friend (a female Muslim physician) to discuss her menstrual problems. She had been bleeding on a fortnightly basis for the previous few months. This was causing havoc with prayer routines because on each occasion she had stopped praying. She was advised that she should continue praying because the pattern of bleeding was unlikely to represent menstrual bleeding. It was suggested that she see her physician for further investigation. Thus far, she had avoided consultation. Contributing to her apprehension were the prospect of not being able to see a woman physician, difficulties in articulating the real reason for her attendance, and the possibility that an internal examination may exacerbate her bleeding.

FEMALE GENITAL TRACT MUTILATION

Female genital tract mutilation is a practice that is carried out in many regions of the world, including some Muslim countries. This practice is most widespread in parts of Africa, stretching in a band from the Horn through Central Africa and extending to parts of Nigeria.[15] The custom's exact origins are uncertain, but it almost certainly predates the arrival of Christianity and Islam to these regions. Female genital mutilation is currently illegal in many countries, including Britain.[16]

The procedure has different forms and is typically done at the age of 6 or 7 years. The least invasive of these involves removing only the prepuce of the clitoris. Removal of the clitoris, or more extensive procedures, is not approved by religious teaching[17]; nonetheless, these extreme practices continue in some Muslim regions largely because of the strong influences of tribal and regional custom and tradition. The most extreme form, infibulation, involves excising the clitoris, the labia minora, and the medial aspect of the labia majora. The sides of the vagina are then sutured, leaving a small opening for the passage of urine and menstrual flow.[16] An intermediate form involves removing the clitoris either partially or totally, together with a portion of the labia minora.

The removal of large amounts of genital tissue can cause considerable problems, including difficulties with micturition, recurrent urinary tract infection, dyspareunia, and dysmenorrhea. The emotional and psychological ramifications of such bodily assault are also now being appreciated.

Traditionally, a local midwife performs a deinfibulation immediately after marriage, thus allowing consummation to occur. The recent large-scale migration from Somalia, Sudan, Eritrea, and Ethiopia to parts of Europe has highlighted the difficulties and problems involved with caring for infibulated women. Access to deinfibulation is restricted in the United Kingdom, and women will, therefore, often become pregnant while infibulated, hindering their care in pregnancy and in labor.

CONTRACEPTION

Many traditions of the Prophet Muhammad extol the merits of marriage, procreation, and fecundity.[18] Muslim opinion with respect to contraception is divided, a minority arguing that it is categorically prohibited whereas the majority opinion is that contraception is allowed but discouraged.[19] A small minority, confined largely to academic circles, suggests that effective family planning strategies are essential to prevent the global overspill predicted by many in the West.[20] The prevalence of contraceptive use in Muslim countries varies widely, reflecting these divergent views, and ranges from less than 5% (in Mauritania, North Yemen, Somalia, and Sudan) to more than 50% (in Turkey, Lebanon, and Tunisia).[21]

VIGNETTES

The following vignettes illustrate some of the challenges encountered in the West when dealing with Muslim patients.

Parental rights

On joining the Muslim community, I was astonished that so much emphasis was put on my relationship with my parents. Here are a few sayings of Muhammad on this subject to which I was exposed almost immediately:

> May his nose be rubbed in the dust! May his nose be rubbed in the dust! (An Arabic expression denoting degradation). When the Prophet was asked whom he meant by this, he said, "The one who sees his parents, one or both, during their old age but does not enter Paradise" (by doing good to them).
>
> A man came to Muhammad and asked his permission to go to battle. The Prophet asked him, "Are your parents alive?" The man replied "Yes." The Prophet responded, "Then strive to serve them."[22]

Support networks

A 28-year-old woman consulted with a physician because of many "aches" and "pains," suggesting a strong psychological component to her symptoms. When her notes were reviewed, it transpired that she had had 3 consecutive stillbirths, the last being only 6 months previously at 36 weeks' gestation. The possibility of the stillbirths contributing to her current condition was raised. She acknowledged this, saying that she had been coping well while in Pakistan because there she had the support of her extended family. On returning to England, however, she found herself more isolated and was struggling to cope. The option of counseling was discussed but was strongly declined. "What has happened to me is a test from Allah and something I will come to terms with. Counselors cannot understand this."

Family responsibility to aging members

> Things are not like they used to be. There is an increasing trickle of Muslims entering nursing homes, and I've actually been thinking of opening a home specifically for Muslims.
>
> Muslim nursing home proprietor

An elderly Bengali man was recovering in a hospital from an episode of pneumonia. He was bed-bound, the result of multiple strokes. On the geriatric team's prompting, the family was approached by social services to discuss a nursing home placement. The family explained that they would prefer to look after him at home. With the support of his physician and social services, he was able to stay in the family home until his death a few years later.

Any questions?

At a seminar on transcultural medicine, junior physicians were asked if they had any particular questions about Islam. Anonymous responses were encouraged to allow the physicians to raise issues of genuine concern without fear of offending the group leader (a Muslim). Two themes dominated: women's rights and fundamentalism.

Barbed wire

Zara, a 27-year-old housewife from Sudan, attended for a follow-up appointment at her local hospital. Her physician was on leave, so she was seen by a locum tenens replacement. On entering the patient's room, the physician extended his hand. Zara politely declined, but failed to give her reasons for doing so. The resulting consultation was tense and dysfunctional.

You earn too much!

Mrs Mu'min attended as an "extra" toward the end of a busy morning surgery. An accountant, she was the principal breadwinner and brought home a healthy wage. Her husband, a doctor trained in Somalia, was unable to practice his craft because his qualifications were not recognized in the United Kingdom. During the last 3 years, he had been forced into various manual occupations. The reason for her consultation? Confused, distraught, and visibly shaken, she explained that her husband was threatening to leave her unless she gave up her job.

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COMMENTARY

American health care professionals should respect the traditions of other cultures

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One of the issues that Dhami and Sheikh raise in their article is that of gender and women's rights. What is most obvious to a feminist American mentality is the way that Muslim women are kept segregated from men by both their clothing and their behavior. Nurses have told me of many cases that illustrate the role of gender in Muslim culture. One is of a Muslim man who tried to keep laboratory technicians from drawing blood from his wife's arm before surgery, relenting only when he completely covered his wife's body, leaving just her arm exposed. Another is of a Muslim man who brought his pregnant wife to the hospital with vaginal bleeding, only to leave when no female physician was on duty to examine her.[1] Frequently Muslim husbands will answer physicians' questions directed to their wives, rather than allowing them to speak. American medical students are often taught that such behavior is a sign of possible abuse. Such cases may leave some American health care professionals with negative attitudes toward Muslim patients.

I suggest another way of looking at this issue. A Middle Eastern woman in my nursing class said that as a Muslim woman, she felt highly regarded. She felt that she was "put up on a pedestal." Because family honor is one of the major Muslim values, and the purity of women is the key to family honor, women have an important place in Muslim society. We should remember that from a Muslim perspective, women are highly valued.

One of the more interesting books I've read on women in Islam is called *Nine Parts of Desire.*[2] The title comes from the Islamic belief that Allah (God) created sexual desire in 10 parts; he gave 9 to women and only 1 to men, which is why women's sexuality must be controlled. Mohammed began the segregation of women to protect his wives from scandal. Others, wanting to emulate the great prophet, followed suit. The author tells of a young professional woman in Gaza who had chosen to wear the hijab—the veiled Islamic dress. When questioned about her choice, the woman explained, "Before I put on hijab, I used to be afraid of everything; afraid of ghosts, afraid of being alone in a room. When I put it on, the fears vanished." Another professional woman talked about how the hijab gave her a sense of freedom—allowing her to be listened to, and allowing her words to be judged on their own merit, without the listener being distracted by her physical appearance.

If a man walks in front of a woman, is he doing it to show his dominance over her or to protect her by finding the potholes in the road? The issue of women in Muslim culture is a complex one, and it is important that health care professionals be nonjudgmental and respectful of the traditions of other cultures.

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Medical Myth

Myth: idiopathic wounds are often due to brown recluse or other spider bites throughout the United States

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INTRODUCTION

Spiders, especially brown recluses (*Loxosceles reclusa*) (figure 1), are frequently incriminated as causative agents in idiopathic wounds, even though diagnoses are usually made solely on the basis of dermatologic symptoms. Rarely is a spider seen inflicting the wound or captured while biting, and it is difficult to either prove or disprove spider participation in the event. The biologic distribution of the brown recluse and related recluse species indicates that many diagnoses made on cases occurring in the western United States are incorrect.[1]

SOURCES OF INFORMATION

Because of my research interests in spider identification and medically important spiders, I have been avidly studying recluse spiders and their occurrence in the western United States. My experience is greatest in California, but the information presented here is pertinent to northern and western states as well. In almost a decade of research, I have found verification of fewer than 10 brown recluse specimens in California in more than 40 years of records. Sources include medical and arachnologic literature and correspondence with scores of arachnologists, county entomologists, vector control personnel, and the California Department of Food and Agriculture, which handles all exotic pest identifications in the state. Most verified specimens were individuals intercepted from facilities receiving goods from out of state. There are no populations of brown recluses in California.

Figure 1 Dorsal view of the brown recluse spider, *Loxosceles reclusa*. The most consistent diagnostic feature for identification is the pattern of 6 eyes, grouped in pairs, with 1 anterior pair and 2 lateral pairs (most spiders have 8 eyes in 2 rows of 4). Although the violin pattern on the cephalothorax (body part to which legs attach) is commonly mentioned as a diagnostic characteristic, this feature can be indistinct or absent in immatures or in related recluse species. In addition, the abdomen is always monochromatic but can vary from tan to dark brown.

MISDIAGNOSIS OF IDIOPATHIC WOUNDS

Despite the lack of brown recluse spiders in California, several hundred cases of "brown recluse bites" have been reported to me in the past decade. Undoubtedly, this is only a small fraction of the total number of brown recluse bites that have been diagnosed. Although it might appear intuitive from figure 2 that these bites could be caused by the native desert recluse (*Loxosceles deserta*), which lives in the comparatively sparsely inhabited southeastern quadrant of California, virtually all so-called brown recluse bites have come from coastal regions with a concentrated human population. In particular, many originate from the San Francisco Bay-Sacramento area, which lies north of the native desert recluse distribution (figure 2) and has never supported a population of any recluse species. Similar scenarios have emerged from other states, cities, or regions—Vermont, New York, Pennsylvania, Florida, Chicago, South Dakota, Colorado, northern Nevada—where recluse spiders are extremely rare (<10 ever collected) or have never been documented.[2] There are published California accounts of 2 "brown recluse bite" case histories from a city where recluses have never been collected[3] and a physician misidentification of a common spider as a brown recluse, captured while biting a child.[4] Brown recluse bites are overdiagnosed in coastal and Northern California.

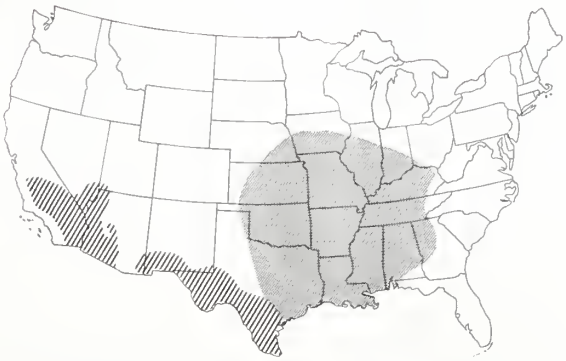

Figure 2 Endemic distributions of the brown recluse (stippling) and related recluse species (lines) in the United States, based on Gertsch and Ennik.[2] Recluse populations become sporadic on either side of the demarcating range borders.

CONDITIONS THAT CAN CAUSE NECROTIC WOUNDS AND/OR THAT HAVE BEEN MISDIAGNOSED AS BROWN RECLUSE BITES

Many conditions can cause necrotic wounds that have been misdiagnosed as brown recluse bites.[5-7] Many of these are disease states in which an arthropod was not involved (box).

If arthropods are in fact implicated, physicians should not immediately think of accidental spider bites as the likely cause. Instead, they should consider creatures that seek mammals for blood meals—such as ticks, fleas, bedbugs, and assassin bugs—and whose bites can cause a variety of reactions.[5,6]

Tickborne Lyme disease can cause a "bull's-eye wound," which is a diagnostic symptom of brown recluse envenomation, and so Lyme disease can be misdiagnosed as a brown recluse bite.[8] Although Lyme disease occurs at low incidence in California,[9] because it can lead to irreversible neural and cardiac complications, its misdiagnosis as a brown recluse bite could have grave consequences.

Conditions that can cause necrotic wounds and/or that have been misdiagnosed as brown recluse bites

- Infections with *Staphylococcus* or *Streptococcus* species
- Herpes simplex
- Herpes zoster
- Erythema multiforme
- Diabetic ulcer
- Lyme disease
- Fungal infection
- Pyoderma gangrenosum
- Lymphomatoid papulosis
- Chemical burn
- Poison ivy/oak dermatitis
- Squamous cell carcinoma
- Localized vasculitis
- Syphilitic chancre

OTHER DIAGNOSES MAY COEXIST WITH SPIDER BITES

Even in cases of verified spider bite, differentiation must be made between toxic effects of venom and secondary infections, such as incurred when pruritus leads to scratching. Furthermore, rigorous clinical investigation might reveal alternative causative agents. For example, in 1 case report, a large spider bit an Australian woman, and therapy for the spider bite was ineffective. Subsequent screening determined that the "necrotic arachnidism" was actually a fungal infection called sporotrichosis,[10] another condition misdiagnosed in the United States as brown recluse bite.[5]

OTHER SPIDERS IMPLICATED IN WOUNDS

Since the early 1980s, a European native, the hobo spider (*Tegenaria agrestis*), has been implicated in necrotic lesions.[11] Although it lives in the Pacific Northwest, east to Montana and south into northern Utah, hobo spider bite diagnoses have already been made in California, even though it has never been documented in the state. The bite of the yellow sac spider (*Cheiracanthium mildei*), another European native, is usually minor but can cause mild necrosis.[12] It was uncommon in the United States before 1950 but has since spread coast to coast, and it is often found in homes.

CONCLUSION

Physicians in nonendemic brown recluse regions (figure 2) should be cautious in implicating brown recluses in idiopathic necrotic wounds. The medical community needs to be aware of the many causes of necrotic wounds that can be misdiagnosed as recluse bites. Culture of specimens taken from wounds might accurately determine the plethora of causative agents of so-called brown recluse bites, which can vary from being arthropod, bacterial, viral, or fungal in nature or due to underlying disease states.

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Poetry

Boundaries

Sometimes they resemble stays
or corsets, designed
to inhibit sexual interference
or breathing.

Sometimes though, they are like skin
protecting from desiccation by
sirocco, sunshine, or scorn.

It is, however, vital that transfer is allowed
of certain substances
to and fro, in order that
balance be maintained
between bursting and shriveling.

If despite our vigilance the barrier is breached
by some interloper, by and large
the foreigner will be evicted
in a flurry of white blood cells.

Sometimes our defenders,
misunderstanding the instruction,
turn their aggression inward, lose touch
with the strategic overview.

But sometimes
for reasons not entirely clear,
we tolerate a foreigner within,
allow his growth at our expense,
protect him from ourselves.

If he brings new life, well
and good; or at least benign invasion.
But beware the smooth stranger who brings
slow death by subversion.

The best we can expect, it seems, is tenuous:
some kind of deal or quid pro quo -
for woman, body, cell or nation-state,
temporary, maybe, hard-brokered for sure,
founded mainly on uncertainty and vigilance
and driven forward by some rash hope
of immunocompetence,
and perhaps, integrity.

Sandy Goldbeck-Wood
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A community left behind

Dorothea Lange/Library of Congress

A dust bowl farmer and his young son driving their tractor near Cland, New Mexico. Rural America has one fifth of the nation's population, but only one tenth of its physicians. Rural communities continue to be poor in health care resources.

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Unhealthy trends in the diet of US teens

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This month in wjm

There are worrying trends in the diet of US teens

The diet of teenagers is an important determinant of their subsequent risk of cardiovascular disease and cancer. Cavadini and colleagues examined adolescent food consumption from 1965 to 1996. An analysis of dietary intake data from 4 nationally representative US surveys of 11- to 18-year-olds showed an increase in the consumption of soft drinks and a decrease in the consumption of raw fruits, nonpotato sources of vegetables, and calcium-rich dairy sources. On p 384, Stang discusses the clinical implications of these trends.

Recreational drugs have serious cardiac side effects

Whereas the neurologic complications of substance misuse are well recognized, few physicians are aware of the cardiac risks. On p 412, Nolan and Ghuran review the cardiac and circulatory changes that these drugs can induce. For example, cocaine, amphetamine, and "ecstasy" can cause hypotension, myocardial infarction, and arrhythmias. All physicians, they say, should suspect substance misuse in any patient with unexplained cardiovascular symptoms.

Constipation has had a historic hold over the public mind

Earlier this year, an article in *The New England Journal of Medicine* shocked the US public. High-fiber cereals were found to have no protective effect against colorectal adenomas. Is this the end of the "high-fiber feeding frenzy"? Probably not, argues Whorton in his witty account of bowel irregularity through the ages (p 424). Constipation has long been thought to cause self-poisoning, he says, and this belief will be hard for society to give up.

Ritalin is prescribed as a "quick-fix" solution

Ritalin (methylphenidate) is in the news again, this time because of allegations that the pharmaceutic industry conspired with psychiatrists to heavily market the drug for attention deficit disorder. Is the disorder being overdiagnosed because of industry pressure? On p 366, Diller argues that pharmaceutic handouts for research and advertising—first to physicians and now to families—has had a huge influence. It is easier for physicians to prescribe a drug as a "quick fix," he argues, than to work with families and schools to address behavioral problems.

Editor's pick

Physicians' communication skills are improving. Most of us have had at least some formal training in breaking bad news, in dealing with angry patients, and in negotiation techniques.

But one area that has received little, if any, formal attention is providing guidance to our patients who want to talk to loved ones about their serious illness. At the time of diagnosis, our patients are emotionally upset, confused about the medical facts, and uncertain about possible outcomes. The newly diagnosed often have multiple roles as patient, worker, spouse, and parent. Research suggests that when given a new diagnosis of cancer, people fare better when they have the support and understanding of others in their lives.

But should they tell their children about their diagnosis? Barnes explores this fascinating topic through a series of qualitative interviews with women newly diagnosed with breast cancer (p 385). The findings are encouraging, reinforcing previous work that stresses the importance of honest discussion to reduce anxiety levels and misconceptions and to improve trust. Controlling or limiting information to children to protect them may have the opposite effect. Given that many malignancies and other threats to life occur during child-bearing years—nearly 30% of cases of breast cancer occur in women at child-bearing age—discussions with parents around sharing a difficult diagnosis with family should become a regular part of our work.

Perhaps no topic is more difficult to discuss with parents than withdrawing medical support from a critically ill child. Children are not supposed to die, and we are ill prepared to deal with their deaths—as health professionals and as parents. Tournay provides a common-sense approach to dealing with palliation and withdrawal of life-sustaining treatment in children (p 407).

Last, on p 368, Emanuel reminds us that living wills remain underused. They need to become a regular part of the doctor-patient checklist.

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Point-Counterpoint

Your spouse/partner gets a skin infection and needs antibiotics: is it ethical for you to prescribe for them?

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Yes: It is ethical to treat short-term, minor problems

Although physicians commonly treat their spouse, partner, or members of their own family, there is ethical concern about the appropriateness of doing so. Under certain circumstances, it is ethically permissible to treat one's family members. Clearly, emergent care, such as cardiopulmonary resuscitation, should be provided as it would customarily to anyone in society, regardless of the relationship between the physician and the injured. The matter becomes more complex, however, when the symptoms are nonemergent, yet possibly indicative of a serious disease process, or when the diagnosis is out of the scope of one's clinical skills.

The Council on Ethical and Judicial Affairs of the American Medical Association has considered this matter and determined that as long as the condition is a short-term, minor problem—such as the skin infection described in the given scenario—it is ethically permissible for a physician to treat family members.[1] These guidelines are also supported by investigators who have studied this common practice.[2]

In their analysis of the practice patterns of more than 400 medical staff physicians, researchers found that 99% of physicians had received requests from family members for medical advice or therapy. Of these, 83% reported that they had prescribed medication for a family member, and 72% reported that they had conducted a physical examination. Investigators concluded that if physicians decide to treat their family members, their judgment must be sound, they must have the appropriate medical data available to them for decision making, and they require the proper training and skills for the matter at hand.

We realize that some physicians are concerned about prescribing for family members. Because of the personal relationship between the parties, the patient may not fully communicate the problem. Alternatively, the patient may try to pressure the physician into prescribing medications. Physicians, on the other hand, may feel guilty about ignoring their family members' symptoms, feeling the need to treat them to maintain a positive relationship. A more serious problem with treating a relative is that the personal relationship can interfere with a thorough assessment of the problem and objective determination of the optimal therapy.

Despite these concerns, it is entirely appropriate for physicians to prescribe for family members, provided that several conditions are met. First, the ailment should be within the physician's scope of expertise. Second, the physician should not accept any limitations on having access to the patient for history taking and physical examination or to the patient's medical record. The physician should be able to get honest answers to any medical questions, such as sources of exposure to an infection. Third, having decided to treat, the physician should know enough about the appropriate therapy to feel comfortable with its use. Finally, once treatment has been initiated, follow-up is essential. If the condition is not resolving as expected, the family member should be referred to another source appropriately.

If these conditions cannot be met, it is preferable that the partner-spouse be referred to his or her personal physician, or it may be appropriate for a specialist—in this case, a dermatologist—to handle the case.

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Bouchard/SPL

No: Such treatment rarely leads to comprehensive care

It is within the natural and acquired disposition of physicians to help patients with their illnesses. When the patient is a spouse or partner with a skin infection, the tendency to want to initiate antibiotic therapy is understandable. This inclination is motivated by genuine concern for the partner, but it may also be fueled by the daily habit of intervention and treatment. Other possible reasons include the easy accessibility of a house call and prescription drugs, a desire to reduce the inconvenience of the partner having to arrange a clinic visit, a desire to eliminate the paperwork of insurance forms or bills, or an attempt to minimize work for overworked colleagues.[1] Such treatment, however, may violate common principles of ethics and good clinical practice.

Treating a skin infection is not, of course, the equivalent of administering cardiopulmonary resuscitation, the Heimlich maneuver, or indeed, any immediately lifesaving procedure to a partner for an emergent medical problem. In these clinical situations, lifesaving intervention is clearly appropriate. In treating a skin infection, however, the potential is there for inadequate diagnosis and mismanagement. This can occur for several reasons.

First, a partner-physician relationship is rarely conducive to the delivery of comprehensive medical care because many of the inherent features of a good physician-patient relationship are often sidelined. For example, the quality of care is higher when a physician maintains a detached and impersonal judgment of a patient.[2] Partner intimacy makes this inherently difficult.

Second, because of the very personal partner bond, the physician may assume—incorrectly—an awareness of all the medical details of the infection simply because of the daily cohabitation and presumed understanding of the partner. As a result, relevant clinical features, such as cause, circumstances, and duration of the skin infection, may be assumed, inferred, or even ignored.

Third, what if the skin infection is a manifestation of a sexually transmitted disorder or part of a systemic illness? Can an objective examination of the partner really be conducted in this situation? For better or worse, house calls are not part of physicians' routine training or daily experiences. Denying a partner a full medical assessment—a thorough history taking, a full physical examination, and suitable laboratory testing—means that the physician is providing substandard medical care.

Finally, other essential features may be overlooked in treating a partner. These include formal follow-up assessments, monitoring adverse reactions, assessing compliance, and objectively reassessing for poor or unpredictable outcomes. I have often received calls from physicians who have treated their partners with 1 antibiotic, then changed to another antibiotic for reasons of inefficacy or because of adverse effects, leaving the partner with an unsure or incomplete outcome. They ask me, "Could you treat my partner, please?" Was it the wrong diagnosis or antibiotic, the unassessed compliance to therapy, or the lack of appropriate follow-up and corollary testing that resulted in the poor clinical outcome?

Clearly, physicians should avoid treating partners' conditions except in emergencies.[3(p12)]

Boucharlat/SPL

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Op-Ed

The Ritalin wars continue

The pharmaceutical industry's effect on prescribing of methylphenidate has been profound

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Ritalin (methylphenidate), the drug used to treat attention-deficit hyperactivity disorder (ADHD), cannot stay out of the news. Class-action suits filed recently in New Jersey and California allege a conspiracy between the pharmaceutical industry, physicians, and the leading ADHD self-help group to unnecessarily medicate American children with a dangerous drug. This news came at the same time that 200 child mental health experts met in Washington, DC, for a 2-day conference sponsored by the Surgeon General on children's mental health. This conference, and another at the National Institute of Mental Health (NIMH), was a direct response to national concerns raised by a report last spring of an alarming increase in the use of Ritalin in toddlers. First Lady Hillary Rodham Clinton was the most conspicuous voice asking questions. But what is the parent of a child who is struggling in school to think about Ritalin?

Ritalin is the best known of the stimulant class of drugs that have been used for more than 60 years to treat childhood hyperactivity, now called ADHD. Myths abound about Ritalin, and the debate over the drug quickly verges on hyperbole. For example, few know that Adderall, a purportedly "new" concoction of amphetamine, has surpassed Ritalin as the most widely prescribed medication for ADHD in annual prescriptions in America.[1] All the stimulants used for ADHD, including methamphetamine, have essentially the same effects and side effects, differing mainly in their duration of action.[2]

Most people continue to think that stimulants, like Ritalin, work paradoxically on hyperactive kids to calm them down. Many studies have proved otherwise: stimulants like Ritalin work the same in children and adults—whether or not they have ADHD—to improve their ability to focus on tasks that are difficult or boring.[3] Therefore, prescribing Ritalin as a way to diagnose ADHD is absurd because everyone's performance improves with its use.

Higher doses of Ritalin speed up children as well as adults. Children, however, do not tolerate these higher doses, nor do they self-medicate. Adults do, and therefore, they are at risk for stimulant abuse and addiction. Children never become addicted.

What about this civil class-action suit? The attorneys are modeling their charges on the recent successful litigation against tobacco companies. But there is a major difference between Ritalin and tobacco. Unlike tobacco, the medical establishment—most notably the American Psychiatric Association along with the main professional child psychiatry association—solidly backs if not promotes the use of Ritalin for ADHD. The vast bulk of scientific literature supports the short-term effectiveness and safety of the drug. Is the pharmaceutical industry suppressing information to the contrary? Rumors abound, including a counterrumor that this action is terribly reminiscent of Scientology-inspired suits in the late 1980s that temporarily led to decreases in Ritalin use in certain parts of the country.

Only the disclosure that comes with discovery will determine whether a Ritalin conspiracy exists. But even without a conscious plan, the influence of pharmaceutical

Malcolm Willett

industry dollars for research support and advertising—first to physicians and now directly to families—has been profound. The market forces of Adam Smith's "invisible hand" operate within the world of childhood mental health and illness. American psychiatry's infatuation with the brain coincides with a drug industry more than happy to contribute funds for research that only counts symptoms and pills. If only family counseling or special education rewarded stockholders the same way Ritalin or Prozac [fluoxetine hydrochloride] does.

Practically every researcher in ADHD now accepts drug company money, as do the self-help groups for at least a part of their work and projects. They would say that they are not influenced by the source of their funding. However, many worry otherwise, from the physicians at local hospital grand rounds listening to a lecture "supported in part by drug company X" to the editors of the *New England Journal of Medicine* reviewing the latest research findings.[4] And the economics of managed care drives physicians toward prescribing Ritalin as a "quick fix" because talking to parents and working with schools simply take too much time.

The "success" of Adderall, which was vigorously marketed to physicians, is more a sign of "hype" activity than any real medical breakthrough. The advertising for the new stimulant product for ADHD, Concerta, crosses new marketing boundaries because it is the first prescription drug for a childhood psychiatric condition marketed directly to parents. The picture of a smiling boy holding a pencil surrounded by his happy parents and sister tells you that they're pleased because the boy is now being treated for ADHD, a biologic disorder best treated with a pill. Such presentations can only further promote a brain-based view of behavior. They ignore and deny the importance of the environment—family, school, neighborhood, and culture—in a child's healthy emotional development.

The NIMH conference set out a course to specifically study ADHD and Ritalin use in toddlers. But virtually every researcher at that conference receives funds from the pharmaceutical industry. At the Surgeon General's conference, it was clear that nondrug approaches to children are egregiously underfunded. What about taking yet another cue from the tobacco wars and developing a tax on either pharmaceutical profits or the drugs themselves that would be directed to other effective interventions for ADHD, like parent and teacher behavioral management training? Specific tax incentives and disincentives are the most likely way that the public, through government action, will be able to influence otherwise powerful economic forces that push toward only medicating for children's problems.

Parents should feel that they can still choose Ritalin safely for their child after they have fully explored issues of family, learning, and school. These new civil suits will only confuse and frighten undecided parents. Unfortunately, given the massive effort to convince America that their children's brains are bad, only such extreme countermeasures like the Ritalin suit may get the public's attention.

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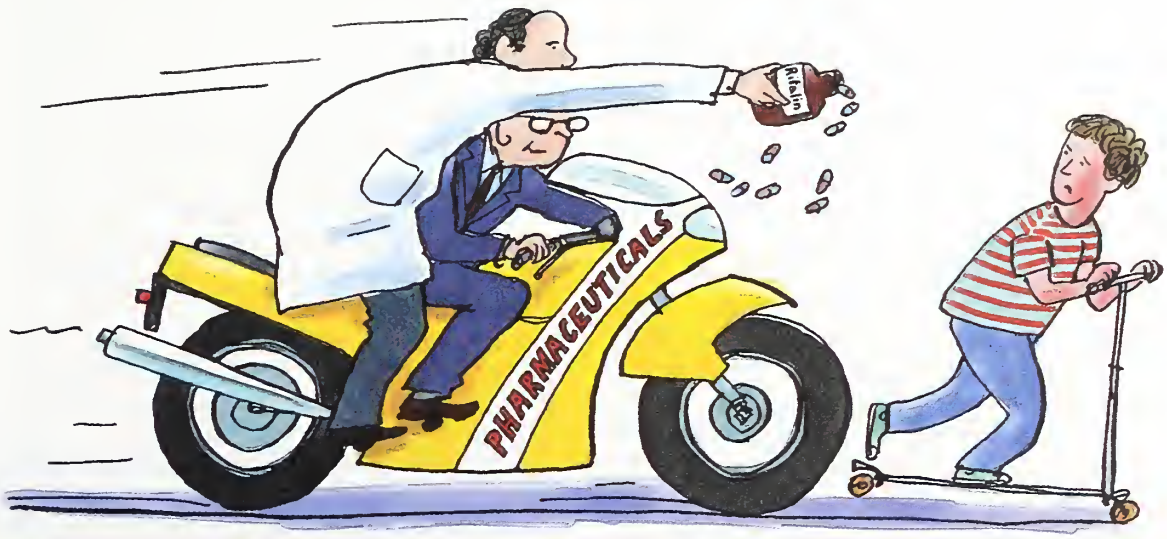

Malcolm Willett

Living wills can help doctors and patients talk about dying

They can open the door to a positive, caring approach to death

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Many people are unaware of living wills but are highly interested once they hear about them. Schiff et al described finding that elderly inpatients are confused by the term "living will," but most would welcome the chance to discuss issues about facing the end of life, and many would want to limit their health care if they were terminally ill.[1] In an assessment of the understanding of living wills in the United States some time ago, a similar state of affairs was found.[2] This juxtaposition of ignorance and interest raises an important question: What is this apparent appetite to discuss and prepare for dying?

When lawyer Louis Kutner proposed the notion of a living will in 1969, he was responding to the fear that technology was driving physicians to impose life-sustaining treatment on patients who might not want it. The living will was seen as a simple device to allow patients to say no, even if they were too ill to communicate. The first living wills used phrases such as avoiding "heroic treatment" in the face of a "hopeless prognosis," and states passed legislation to give legal sanction to physicians honoring such directives throughout the United States. But physicians found difficulty translating these dispositions into specific treatment choices. A new wave of work began: the development of validated worksheets.[3]

It is difficult to turn subjective phenomena such as a person's values and goals for care in hypothetical scenarios into objective criteria. But psychometricians have set out a series of standards for the valid framing of topics and for eliciting and recording opinions, wishes, and reasoning.[4] So the living will movement, which aimed to elicit preferences on how decisions should be made and by whom, tried to apply these standard procedures.[5-9] In the process of developing validated forms, it became clear that they needed to be used as worksheets to facilitate discussions and the making of decisions.[10]

Moving away from the notion of a legal defense against aggressive physicians, the living will movement realized that it is the process that is the central issue. The main outcome was to honor the best available portrait of patients' desires. A good process had to do with several more things: the patients having a chance to consider and have some control over their last chapter of life, the proxy decision makers being ready for their roles, and the families having a chance to talk about issues relating to end of life and to resolve personal matters. Dying, it emerged, was a taboo topic that patients and families wanted to repossess.

But studies showed that living wills did not achieve their goal.[11] Some commentators advocated dropping the whole idea. Meanwhile, the hospice movement and palliative care services were gaining prominence, and pioneer clinicians were trying to integrate both concepts into medical practice.[12,13] Both movements accepted advance care planning as central to their philosophy of total care.

Eventually, living wills came to be seen as a vehicle for achieving greater wisdom and skill in a fundamental aspect of health care and a civilized approach to mortality. Advance care planning is a process of discussion, a component of care. Worksheets are for helping reflection and deliberation and for team building between the professionals and families and the patient. Legal documentation has a small but legitimate role. The outcomes are quality experiences for dying persons and for those caring for them. Most people facing terminal illness want to secure dignity, comfort, control, and a chance to leave a purposeful legacy. They do not want to burden their loved ones. Advance care planning with quality care at the end of life can, if done well, provide these things for most people.[14]

Yet, few physicians or patients initiate discussions on advance care planning. Possibly a natural ceiling exists, in that only about half of patients have estate planning wills, let alone living wills.[15] But progress may be hard to measure and better than we think. The best discussions and plans for care may never be documented in a discrete, recognizable living will. Desired outcomes of peace and resolution are hard to measure and hard to compare with a suitable control group.

It is likely that most of us could improve the way we talk with, plan with, and care for patients and their families as they approach death. Validated worksheets need to be developed for different populations. Outcome measures for quality care at the end of life will need to be more sophisticated and focused on subjective, meaningful experiences of patients and families.[16] Skills in breaking bad news and sharing decisions can be adapted for different cultures; skills in discerning the needs of the proxy or family and supporting them for the patient can be made suitable as well. Dying is, in the end, normal in all contexts, and the challenge is the same: can we really care for those of us who are facing our last life chapter?

Linda Emanuel is a Professor of Medicine and Director of the Interdisciplinary Program on Professionalism and Human Rights at Northwestern University.

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Rocket science

wjm launches a fast-track system for publishing important papers

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2000;173:369

Have you written a paper that you think clinicians need to read urgently? Do your research findings have immediate implications for public health policy? If so, you may want to take advantage of *wjm*'s new fast-track system by which we can offer rapid peer review and publication of important papers.

This month we feature our first article that has been fast-tracked to publication, as shown by the rocket logo (see box). On p XXX, Ginsburg and colleagues report the results of a survey of physicians from 5 California counties that explores their attitudes toward using cost-effectiveness as a component of their clinical decision making. Nearly all physicians believed that there was a legitimate need for cost containment in today's health care environment. No surprises there. But when questioned further, more than half believed that a physician has a duty to offer any intervention with a marginal benefit, regardless of its cost. Physicians recognize that resources are limited, but many aren't willing to accept their own role in negotiating tradeoffs between the costs and benefits of medical treatments. Although the study has a number of methodologic limitations—discussed by Hoffman and Wilkes in their commentary on p XXX—it focuses our attention on the pressing issue of cost-effectiveness.

Why did we fast-track the paper? The study forms part of a regional project called Visible Fairness,* initiated by the nonprofit organization Sacramento Healthcare Decisions. This month, the project will involve the local media and the public in a debate about which medical interventions should be paid for, and which should be denied, by providers. It wants providers to make decisions that are "fair" and "visible" to the public. We thought that fast-track publication of the study would help consumers to understand physicians' decision-making processes and would stimulate urgently needed public, media, and professional debate about cost-containment policies. In addition, we understand that many health plans are considering incorporating cost-effectiveness criteria. They should not do so behind closed doors—all stakeholders in health care must be involved.

Fast-tracking an article has considerable resource implications because it demands time of editors and peer reviewers. It will, therefore, be reserved for only those of great importance, that will change clinical practice immediately, or that have urgent public policy implications. We will not fast-track papers because of an author's eminence, institutional pressures, or any other spurious reason. We envisage fast-tracking a handful of high-quality research papers to publication each year.

If you request fast-track publication, make your reasons explicit. Within 3 working days, we will give you 1 of 3 answers. First, we may reject the paper as being unsuitable for *wjm.* Second, we may decide that the paper does not warrant urgent review, but we would like to put it through our usual editorial processes. Finally, we may agree that it merits fast-track review, and we will have it peer reviewed and considered at our next editorial advisory committee meeting, which is usually within 1 month. If the committee decides that we should publish the paper, we will do so in the next issue that goes to print. You need to be available to make quick revisions to the manuscript.

The system is an experiment that will be evaluated as we go along. If it works, it will lead to *wjm* publishing more "rocket science."

* Details of the Visible Fairness project, including a list of the partners involved, can be found at http://www.sachealthdecisions.org/html/visible_fairness_project.html

Med.Pix

A netlike rash

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QUESTION: A 59-year-old man is seen because of a netlike rash in the sacral area. The rash began 2 months ago and was neither pruritic nor painful. The patient has a long history of arthritis and back pain. On physical examination, a hyperpigmented reticulated rash is seen on the sacral area (figure).

What additional history would help to make this diagnosis?

Netlike rash on sacral area

ANSWER: Additional history revealed that the patient started using a heating pad to soothe his back pain about the same time the reticulated rash began to appear.

The patient has erythema ab igne ("red from fire"), also known as toasted-skin syndrome, heat-induced circumscribed dermal melanosis, fire stains, ephelis ignealis, or livedo reticularis e calore.

Erythema ab igne is a cutaneous disorder caused by absorption of infrared radiation. Women are affected more often than men.[1] Patients have a history of repeated exposures to heat at a lower level than that which causes a thermal burn. The skin is often mildly erythematous initially, but after repeated heat exposures, the classic blue, purple, or brown reticulated hyperpigmentation develops.[1]

Because of the general availability of central heating, erythema ab igne is less common in the United States than in countries where open fires are commonly used for heating. Historically, this condition was often seen on the inner thighs and legs of women who sat in front of a stove or open fire.[1,2] Currently, it is most commonly seen in this country following repeated use of hot water bottles, infrared lamps, and heating pads. Erythema ab igne has been reported to appear on the legs following prolonged, daily exposure to a car heater. Occasionally, the first sign of splenomegaly, pancreatitis, pancreatic cancer, and other

cancers is erythema ab igne resulting when patients apply external heat to relieve the underlying pain.[2] Work exposure to heat (such as for bakers, silversmiths, and boiler operators) may cause this condition.[1]

RISK OF MALIGNANT TRANSFORMATION

A small risk of malignant transformation is thought to be present in the area affected by erythema ab igne.[1,2] Carcinoma can develop from dysplastic keratinocytes that are harbored within the reticulated hyperpigmentation. Both squamous cell carcinoma and Merkel cell carcinoma have been known to arise within erythema ab igne. Patients should be evaluated regularly so that any thermal keratoses (similar to actinic keratoses) or other premalignant lesions can be treated appropriately.

DIFFERENTIAL DIAGNOSIS AND TREATMENT

An important disorder to consider in the differential diagnosis is livedo reticularis. Livedo reticularis is characterized by reddish blue mottling of the skin in a reticular pattern. It occurs more often in women. Livedo reticularis may be due to other disorders, including vasospastic conditions, connective tissue disorders, and drug reactions. Unless symptoms are present that are related to an underlying disorder, patients typically have no complaints other than the cosmetic appearance of the skin. In contrast to erythema ab igne, the skin manifestations of the benign form of livedo reticularis resolve with heating. In livedo reticularis that is secondary to another disorder, the underlying disease process should be treated.[3]

No definitive therapy for erythema ab igne is available. Reducing or eliminating exposure to the heat source early in the disorder may reverse the hyperpigmentation.[1] However, prolonged exposure leads to permanent hyperpigmentation and increased risk of malignant transformation. Treatment with topical fluorouracil may be useful in reducing or eliminating dysplasia of keratinocytes.

This patient was instructed to turn down the heat setting on his heating pad and to use the pad less often. On follow-up 2 months later, the hyperpigmentation had decreased.

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News and Features

Laparoscopic surgery: two thirds of injuries initially missed

Annabel Ferriman, London

A study of misadventure data relating to laparoscopic surgery shows that the injury most frequently associated with the procedure is damage to the common bile duct, followed by perforation of the small bowel and of the colon. Injuries occur most often during gallbladder operations, with exploratory laparoscopy coming second.

The data are contained in a report from the Physicians Insurers Association of America, which draws on information from 19 medical insurance companies.

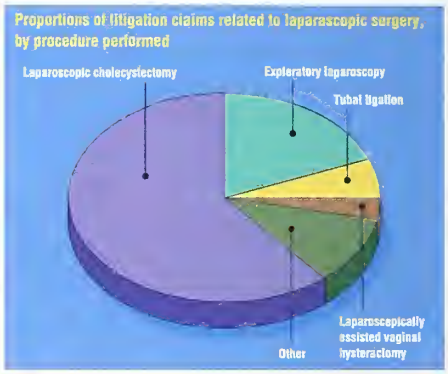
This latest study analyzed data from 535 cases, in which 163 claims were settled, with payments to the plaintiffs totaling $34 million. Payments ranged from $1,500 to $925,000, with the average being $212,350.

Failure to identify the injury once it occurred was a key factor in the severity of the outcome. In more than two thirds of the incidents examined, the injury was not identified until some time after the conclusion of the procedure. In some cases, that delay led to serious complications, such as peritonitis and sepsis. Resulting indemnity payments averaged 10% more when the patient's injury was not recognized before the conclusion of the procedure.

Cholecystectomy injuries were not recognized before the conclusion of the surgery in 83% of claims. Injuries that were recognized tended to be vascular in nature, whereas visceral injuries causing complications were more likely to remain unrecognized until after the end of surgery. Difficulty in visualizing the anatomic structures during laparoscopic surgery was a contributing factor to these types of adverse incidents.

Trocars were the most common type of device causing injury. More than a quarter of all claims cited either primary or secondary trocar insertion as the prime cause of injury. Surgical clips were the second most common reason for injury (9%), followed by Veress needles (8.2%), cautery equipment (5.4%), and sharp objects such as scissors or scalpels.

The average age of patients who died of alleged injuries was 51 years. Deaths commonly resulted from multiple injuries. Perforations of the small bowel and colon resulted in the severest injury, probably resulting from the long delay between the surgical procedure, the discovery of the injury, and the repair.



The report's recommendations included the following: before a new procedure is performed, proper training should be undertaken; indications for using laparoscopic surgery should be documented, contraindications recorded, and the specific reasons why benefits outweigh risks specified; the patient should be evaluated for injuries before the procedure is concluded; and if the surgery is being done on an outpatient basis, the patient or caregiver (or both) should be educated to recognize complications.

Personalized medicine comes a step closer for asthma

Scott Gottlieb, New York

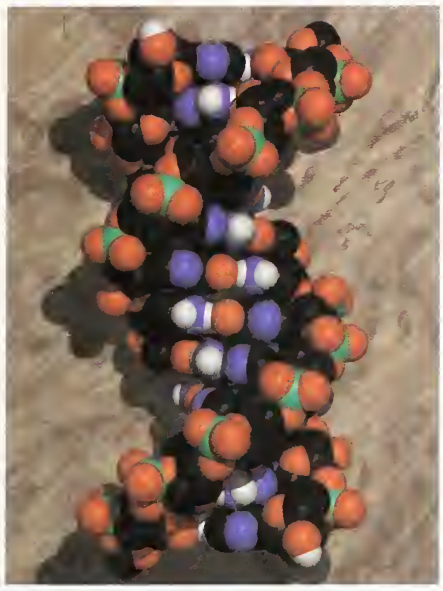
Researchers have discovered subtle differences in the DNA of people with asthma, which help to predict which patients will benefit most from a certain drug before they take it, a new study has reported.

In tests of the DNA of 121 patients with asthma, researchers led by Stephen Liggett, professor of medicine at the University of Cincinnati College of Medicine, and colleagues found 4 different patterns of DNA in a gene that helps to relax muscles in a person's lungs. Lung function was measured before and after treatment with albuterol [salbutamol], with the individual responses correlated to the sequence of variations found in discrete regions of a person's DNA.

Albuterol, a drug that is aimed at spurring the muscle-relaxing gene into greater action to treat asthmatic wheezing, worked well in those with 1 pattern, not at all in those with another, and moderately in the other 2 cases (*Proc Natl Acad Sci USA* 2000;97:10,483-10, 488).

It is the first example, researchers said, of personalized drug treatment, made possible by the sequencing of the human genome. In the future, the researchers said, they will be able to match individual patients to different medications, using their DNA as guidance to improve the drugs' effectiveness and to eliminate harmful side effects. "Pharmacogenomics" is considered the most likely spin-off of decoding the human genome to have practical application in the near term.

Albuterol works by blocking the β_2-adrenergic receptor. This causes muscles to relax and allows bronchial tubes to dilate, aiding the flow of air to the lungs. Identifying the genes that affect the way a person re-



Paul Thiessen/Chemical Graphics

DNA can be used as guidance to improve the effectiveness of drugs

sponds to the drug will help physicians tailor prescriptions for each patient, said Liggett.

"This is a step toward personalized medicine," said Liggett. "The era of 1 drug fitting all is probably coming to an end soon."

The regions in DNA that the researchers were examining are single nucleotide polymorphisms. Some single nucleotide polymorphisms act like typographic errors, causing abnormalities in the DNA, while others do not seem to matter. In this case, researchers had previously found that the β_2-adrenergic receptor gene contains 13 of these sites where single nucleotide polymorphisms are present in the genetic code.

The scientists analyzed all the possible differences people could have and found that 4 common differences predicted how people would respond to albuterol.

Medicines now are generally tested on large numbers of people, with researchers looking at the average response of those taking the drug versus those taking placebo. "You'll see responses that are very, very good and some that are bad," Liggett said. "The FDA says to look at the average response."

As a result, he said, some drugs that may be useful for a small subset of patients may never become available because they show little or no benefit, or they even harm, on the aggregate. By using examinations of DNA, researchers will be able to find subgroups of patients who benefit from certain drugs even if, on average, most patients show no response.

Liggett said that similar genetic studies are now underway for all of the classes of drugs used to treat asthma. Eventually, he said, genetic tests of a patient with asthma will identify those drugs most likely to be useful. From this, a personalized list of probable benefits could be drawn up for each patient and used by physicians to tailor prescriptions. "This would reduce the trial-and-error period that all physicians go through when they have patients with complex conditions," said Liggett.

Online pharmacies: industry growing, but safety questions remain

Amid the "cutthroat competition" in the online pharmacy market, some companies are beginning to develop successful Web-based enterprises, Knight Ridder/*Philadelphia Inquirer* reports. Last year, Americans bought $158 million worth of prescription drugs online, or 0.2% of the $100.6 billion spent overall, leaving "enormous room for growth." The most successful online retailer is Merck-Medco, a subsidiary of Merck and Company. Prescription drugs are available on the Merck-Medco web site (http://www.merck-medco.com) but only to consumers whose health plans also use the company's pharmacy benefits manager component. Merck-Medco also has formed an alliance with CVS.com to distribute their products online to Merck customers.

Another major online pharmacy, Drugstore.com, has formed partnerships with Cigna Corp of Philadelphia and California-based WellPoint Health Networks Inc.

Such coalitions may be the only way that online pharmacies can survive financially. Jim Williamson, an International Data Corporation analyst, noted that "pure play" Internet drug retailers, or "those exclusively devoted to online business," are losing money (Karash, Knight Ridder/*Philadelphia Inquirer,* October 23, 2000; F11). Although Drugstore.com posted "significantly higher" revenues in the first half of this year, the company will report its fourth straight quarterly loss (Piskora, *New York Post,* October 23, 2000; Wealth section).

But is it safe?

As the online pharmacy industry grows, so do concerns about the safety of obtaining prescription drugs through the Internet. Food Drug Administration (FDA) Commissioner Jane Henney said, "Unfortunately, fraudulent or disreputable web sites selling prescription drugs [do] exist." The FDA warns that illegal web sites "may send . . . counterfeit or contaminated drugs, the wrong drug, or an incorrect dose." To prevent such occurrences, several federal and state prosecutors have sought and won injunctions against illegal sites. Last year, the National Association of Boards of Pharmacy created the Verified Internet Pharmacy Practice Sites program, which certifies traditional and online pharmacies by ensuring their compliance with state laws, patients' right to privacy, authentication and security procedures, and quality assurance policies. Richard Hellman, a physician and president of the Metropolitan Medical Society of Greater Kansas City, said, "What we've learned so far is that there are a lot of hazards for people buying things over the Internet. The promises made are not always kept, and the drugs aren't always what people think they are" (Karash, *Kansas City Star,* October 21, 2000; Business section).

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Medicine and Money

Everything you ever wanted to know about your anatomy

Hold on to your clothes and run for cover. Whole body scanners are appearing on vacated land as rapidly as Starbucks. Diagnostic body imaging scans are becoming faster, better, and cheaper.

USA Today recently ran a feature on its cover, "The Inside Story" by reporter Robert Davis, that discussed a 20-minute whole body scan for about $700. Davis had the examination surfside in Newport Beach, California, and the radiologists found "a bump" on his aorta that will apparently have to be monitored. Davis says he is glad he took the test.

Alternatively, you could go to "Inside Trac," in Beverly Hills, California. The 3 leading causes of death in America are heart disease, colon cancer, and lung cancer, so why not get all 3 organs scanned, just in case? An InsideTrac heart scan costs $375. Add the body, and it becomes $795, and for $1,325, you also get the virtual colon study, which uses 3-dimensional reconstruction to exclude cancers and polyps larger than 6 mm. You'll need no anesthesia, laboratory work, or barium, and you won't feel a thing. The folks at InsideTrac say that they can scan you for early signs of disease in a mere 7 minutes.

Many in the medical establishment think that all this is unnecessary, expensive, and wasteful and that any little abnormality will lead to other more invasive, dangerous, uncomfortable, and costly tests. Perhaps they're right. Only time will tell. Our guess is that whole body scanning might someday be performed routinely.

Why not? The current costs of studying multiple anatomic areas are now less than what it originally cost to scan 1 site. Scanning costs are sure to come down even further. It is true that some findings will lead to more tests when indicated, just as in the past, but we can deal with that.

Why not do the tests sooner rather than later while the patient has a fighting chance? Some academic internists would rather make a late but exact diagnosis on the moribund than an early, less-than-perfect diagnosis on someone who is clinically healthy. They often have this scientific principle that asserts that if they didn't have the idea first, invent the technology, do the first studies, or write the first articles, the concept simply doesn't cut the mustard. "Be neither the first to adopt the new," they say, "or to throw the old aside"—unless, of course, it was their idea in the first place. But they have been wrong more than once.

InsideTrac™ offers whole body scanning that is "painless, quick, and affordable"

The commonly held belief that men are more vulnerable than women to death by heart attack or colon cancer is incorrect. In addition, the rate of death of women from lung cancer is quickly approaching that of men. Thus, the scans offer something for everyone.

For the individual patient, the decision will not require complicated cost analyses. For the man or woman who is healthy, wealthy, wise, worried, or anxious, it will be a simple decision of "yes" or "no" to the scans. In fact, as more insurance companies pay for these screenings, their use will become more widespread. Perhaps, heaven forbid, such testing will actually eliminate other expensive laboratory and imaging modalities and reduce medical costs.

If these examinations can relieve anxiety, they could be worth the cost. As diagnostic radiologists, we like the idea of being primarily responsible directly to the patient. When abnormalities (or possible abnormalities) show up, we would refer patients to the appropriate physician or specialist. Perhaps this would be the start of a new trend in which radiologists would act as primary care physicians. We would certainly make sure that other physicians sent the patient back to us, the referring physicians. Let's call it vindication for the sins of the past when referring physicians took credit for our diagnoses.

In the managed care arena, these scans might appeal to the for-profit mass marketers, after they have done their inevitable marketing studies and focus group analyses. One week, for example, they might offer a special rate on a heart scan. The next week, it might

be a 2-for-1 and the next a 3-for-2 rate. Such great deals! Eventually someone will invent a handheld scanner like Doctor McCoy used in *Star Trek*. We propose calling it Inside Trac's StarTrec, the "real McCoy."

We know that this technology makes perfect sense on an intellectual basis, and we should probably have these scans done tomorrow. The problem is that we're not sure if we really want to know. But for most patients, this is a matter of personal choice—which is the way it ought to be.

Authors Both authors are recovering diagnostic radiologists who retired just before the barium hit the fan. Michael Arnold Glueck, of Newport Beach (72143.2077@compuserve.com), has written extensively on medical, legal, mental health, and disability reform issues. Robert J Cihak, of Aberdeen, Washington (RCihak@techline.com), is president-elect of the Association of American Physicians and Surgeons.

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A book to make you think

Fevered Lives: Tuberculosis in American Culture since 1870 Katherine Ott, Harvard University Press, $16.95, pp 296, ISBN 0 674 29911 6

In 1992, the *New York Post* ran the headline: "TB time bomb. Homeless contaminate public areas in city." This headline encapsulated much of the city's anxiety about the resurgence of the public health threat that is tuberculosis and the cultural forces that influenced the response. The recent epidemic in New York resulted in a reassessment of the role of public health officials, greater awareness of clinicians to drug-resistant strains and nosocomial spread within homeless shelters, prisons, and hospitals, and an increased public awareness of an ancient disease that many thought had been eradicated in the West. In the late 20th century, American society, and in particular New York society, re-evaluated its relationship with tuberculosis. And many of its responses were mirrored in the past.

In *Fevered Lives*, first published in 1996, Katherine Ott traces the cultural transformation of tuberculosis in America from 1870. She describes the changing "layers of meaning" that surrounded a diagnosis of tuberculosis and how, among the middle classes, this "most flattering of all diseases" of the 1870s was, as awareness of the social associations grew in the 1880s, transformed into a disease that was the consequence of either acquired or inherited degeneracy. She also describes how the disease mirrored "ethnic and racial fears and prejudices." For example, many believed that very different disease processes occurred in black people. "The seed of negro consumption is not in the lungs, stomach, liver or any organ of the body, but in the mind." By the turn of the century, however, the enthusiasm for blaming individual weaknesses was tempered by an increasing awareness that society's strictures were in part responsible.

Ott tells a fascinating story in describing the technology associated with medical advances, how these were interwoven with changing responses to and perceptions of disease, and how physicians' authority increased as they cornered the market in interventional expertise and microbiological understanding. At this time epidemiological awareness arising from "data-gathering techniques . . . gave regularity and consistency to understanding of the disease," further contributing to the medical profession's authority. Despite its subtitle ("Tuberculosis in American Culture since 1870"), Ott's book largely concentrates on the period before the 1920s. Somewhat disappointingly, little is made of the advent of effective treatment and the more contemporary issues of drug resistance and the disease's associations with HIV. These issues, and the United States' response to them, have undoubtedly been influenced by past approaches.

In April 1993, increasing rates of tuberculosis led to the World Health Organization declaring a global emergency. As tuberculosis has enjoyed a resurgence, allied as it is to economic and social fractures and the HIV epidemic, so books on the disease are also enjoying something of a revival. The fact that several overlap in the period they cover, the issues they address, and their interpretation of their research findings is perhaps not surprising. Ott, however, offers much that is fresh. She argues persuasively that "the history of tuberculosis chronicles how a romantic, ambiguous affliction became first a dreaded and mighty social truncheon, and finally an entity bound up in the public health and civic order," and she uses powerful images to support her thesis.

Overall, *Fevered Lives* offers interesting insights into doctors', patients', and the public's changing understanding of, and response to, tuberculosis in the United States over a period of dramatic transition, and it describes well how different attitudes were reflected in the changing roles adopted by the different actors in the cultural tableau.

Competing interest: RJC's book *From Chaos to Coercion: Detention and the Control of Tuberculosis* was published by St Martin's Press in January 2000.

Richard J Coker
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Mail

Inequality and political power

To the editor,

There is a well-documented relationship between social inequities and health, and this has led to a search for ways to improve health through addressing these inequities. Is this something that is amenable to scientific study?

In most societies, elimination of injustice has been a recurrent but an unsolved issue. The lack of a scientific perspective has hindered the process. Rawls considers that for justice to exist there must be some kind of re-distribution of resources.[1] A proper allocation of capital, he says, allows valuable investment for the benefit of the most disadvantaged people. Rawlsian proposals, leaving aside the difficulties of their implementation, generate other unsolved utilitarian questions, like the search for the greatest welfare for the greatest number of people. But persistent utopian or rhetorical proposals won't address the problem that the rich are getting richer and the poor are getting poorer.

In her July 2000 Op-Ed, Starfield reminds us that poverty-related health consequences cannot be wholly explained by material deprivation, since they are not alleviated substantially by providing alms to lighten the burden of the poor.[2] We must therefore elucidate the underlying mechanisms linking poverty to illness and find interventions to reduce the effects of inequity on health.

Health and illness have social and political roots, besides the biologic ones. Political power generates an uneven distribution of income because the people in power may act with the assumption that everyone should be dedicated to competition and struggle. Economic power can be the base for further enlargement of personal political power.

I have argued that a better quality of political power may reduce the social vectors that tend to impoverish mankind.[3] A standardized educational program about the appropriate use of political power may lead to refined leadership practice, possibly leading to greater societal equality. It might also be possible—with systematic vigilance and the use of new medical diagnostic tools[4]—to prevent people with psychopathic personalities from occupying leadership positions.[4]

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Severe varicella in an immunocompromised adult presenting with abdominal pain

To the editor,

A 65-year-old woman was admitted to our hospital because of abdominal and right flank pain. She had undergone a splenectomy 5 years before for non-Hodgkin's lymphoma and a cycle of chemotherapy 2 months before her admission.

On physical examination, the patient was afebrile, and her vital signs were normal. Cardiac and pulmonary examination findings were normal. An abdominal examination revealed normal bowel sounds with diffuse tenderness localized to the right half of the abdomen, but with no guarding. There were no lesions on the skin or mucosa.

Results of initial blood tests—complete blood cell count, liver enzyme levels, amylase, and blood chemistries—were in the normal ranges. The chest on radiography appeared normal. Radiography of the abdomen without contrast enhancement showed distention of the ascending colon, and contrast-enhanced radiography showed no obstruction.

The distention of the transverse colon and cecum increased progressively, and on the 4th day a decompressive cecostomy was performed. On the day after, high fever (40°C [104°F]) developed, and the patient became obtunded. She was transferred to the intensive care unit for the treatment of possible sepsis, and antibiotic therapy with imipenem-cilastatin sodium and tobramycin sulfate was initiated. Her neurologic condition deteriorated progressively, and on the 10th day of hospitalization she required intubation and mechanical ventilation.

A vesiculopapular rash developed, beginning on the 7th day. This started on the trunk and face and then spread to the entire surface of the patient's body, sparing the mucous membranes. The vesicular rash became progressively hemorrhagic and purpuric. Her platelet count fell, and the result of coagulation tests became abnormal.

An enzyme-linked immunosorbent assay for herpes zoster virus showed a positive result for IgM and a titer of 640 IU/L for IgG on the 15th day. A regimen of acyclovir was started. The titer of IgG increased to 3,300 IU/L on the 25th day, and hemofiltration was performed for progressive azotemia. On the 29th day of hospitalization, the patient died.

Severe varicella is a well-known complication in immunocompromised children, and intense abdominal pain is often the first symptom of dissemination. We searched the medical literature for this syndrome in adults with MEDLINE using the search terms "varicella," "immunocompromised host," and "abdominal pain" and the option "related articles" for the articles found. In 2 articles, adult immunocompromised patients with varicella presented with abdominal pain as their major complaint.[1,2] In all the cases described, the symptom at presentation was abdominal pain. Fever, the typical mucocutaneous rash, diffuse visceral dissemination, and intravascular coagulation began some days later.

Varicella should be considered in the differential diagnosis of abdominal pain in all immunocompromised patients

Varicella should be considered in the differential diagnosis of abdominal pain in all immunocompromised patients, particularly when the cause is not obvious. Acyclovir therapy should be started as soon as the clinical picture shows the typical manifestation of the disease because surgery in immunocompromised patients is poorly tolerated, and prompt initiation of therapy with acyclovir can be life-saving.

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Competing interests: None declared

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Whatever questions, comments, or other contributions you have, we'd like to receive them. We realize that it's experience like yours that makes the journal come alive. Please send your questions, ideas, or comments to us by email: wjm@ewjm.com.

Original Research

US adolescent food intake trends from 1965 to 1996

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ABSTRACT **Objective** To examine adolescent food consumption trends in the United States with important chronic disease implications. **Methods** Analysis of dietary intake data from 4 nationally representative US Department of Agriculture surveys of persons aged 11 to 18 years (n = 12,498). **Results** From 1965 to 1996, a considerable shift occurred in the adolescent diet. Total energy intake decreased, as did the proportion of energy from total fat (39%-32%) and saturated fat (15%-12%). Concurrent increases occurred in the consumption of higher-fat potatoes and mixed dishes (pizza and macaroni and cheese). Lower-fat milks replaced higher-fat milks, but total milk consumption decreased by 36%. This decrease was accompanied by an increase in the consumption of soft drinks and noncitrus juices. An increase in high-fat potato consumption led to an increase in vegetable intake, but the number of servings for fruits and vegetables is still lower than the recommended 5 per day. Iron, folic acid, and calcium intakes continue to be below those recommended for girls. **Conclusions** These trends, far greater than for US adults, may compromise the health of the future US population.

Adolescence is a critical period during which lifetime habits are established. Many teenagers are preoccupied by their physical characteristics and appearance,[1] resulting in nutritional practices such as dieting or consuming fad foods. Dieting, a common practice among adolescent girls, may be the cause of inadequate dietary intake and may have impottant health effects for selected nutrients such as calcium, iron, and folic acid.[2] Some teenagers continue to exercise and become more involved in sports, while others stop and eventually develop a sedentary lifestyle.[3] Many of the adolescent lifestyle habits may have severe consequences in the long run. For example, being overweight during adolescence is associated with increased risk for being overweight during adulthood[4,5] and for increased incidences of hypertension during adolescence[6] and of adult-onset diabetes during adolescence.[7] The National Health and Nutrition Examination Surveys (NHANES) in the United States showed increasing prevalence of overweight in not only adults but also adolescents, in particular in the past 15 years.[8,9] Furthermore, we know from previous studies that blood pressures and cholesterol concentrations track from childhood into adulthood.[10,11] Excessive weight gain during childhood and adolescence is a determinant of adult cardiovascular risk and mortality.[12,13] Similarly, inadequate fruit and vegetable intake may affect the prevalence of selected cancers.[14] This study was initiated to provide a better understanding of adolescent food habits and to follow food trends that may have implications for the later development of adult noncommunicable diseases.

METHODS

Survey design and sample

From the initial sample of about 90,000 persons participating in 4 US Department of Agriculture (USDA) surveys, adolescents aged 11 to 18 years with dietary data were selected for this study. Of 12,498 adolescents, 3,061 came from the 1965 and 6,208 from the 1977-1978 Nationwide Food Consumption Surveys and 1,656 came from the 1989-1991 and 1,573 from the 1994-1996 Continuing Survey of Food Intake by Individuals (CSFII). The USDA surveys from 1965 to 1991 contain stratified area probability samples of noninstitutionalized US households in the 48 coterminous states and in all 50 states in 1994 through 1996. The 1977, 1989-1991, and 1994-1996 surveyors conducted 4 data collections (winter, spring, summer, autumn), each surveying a different sample, whereas the 1965 survey collected individual dietary data in a single spring sample. These surveys were self-weighting, multistage, stratified area samples of the US population. For each survey, response rates differed at the level of the primary sampling unit. Thus, weights based on response rates for each sample unit are used to permit inferences applicable to the total noninstitutionalized US population. Detailed information on the methods pertaining to each survey has been published previously.[15-18]

Dietary data

Each survey included at least 1 in-home, interviewer-administered, 24-hour dietary recall. The 1977 and 1989-1991 surveys also included 2 self-administered 1-day food records. Information was collected on everything teens ate at home or away. For our purpose of studying trends in dietary intake over time, we used only the first day of dietary intake information from each survey—the 1-day (24-hour) dietary recall. This method avoids the biasing of intake results that may occur because of the different dietary data collection methods used and different number of days of reported intake that were collected.

Two of the challenges in trends analysis are accounting for differences in how foods are defined over time and characterizing the nutrient contribution of each food.

Food codes changed considerably (often for the same food), and technology to measure nutrients has also changed. We have developed several ways to link foods coded and collected in the past decade with foods all the way back to 1965. Values from the 1994 nutrient database were then applied to the 3 data sets before 1994 to provide consistently high-quality estimates of nutrient values over time. In the most recent survey, the nutrient database specific to each survey year was used to calculate nutrient values to reflect changes in foods on the market.

This approach allows the use of newer measures of nutrients and for considering shifts in food descriptors. Changes in the actual nutrient content of foods will not be captured by the use of a single nutrient composition table, and trends may be either overstated or understated. In weighing the advantages and disadvantages of using different nutrient composition measures, we concluded that using the 1994 nutrient data provides a conservative measure of some of the nutrient trends in foods (for example, fat) and allows for the examination of trends in several nutrients (for example, fiber) that would not have been possible otherwise.

The Food Guide Pyramid database released by the USDA with the 1994-1996 survey was used to calculate the servings of fruit, vegetables, milk, and grains and the ounces of lean meat equivalents for all 4 surveys.[19] The same linking program used to apply the 1994 nutrient values back in time was used for these calculations.

Food grouping scheme

To examine changes in the quantity of foods consumed over time, we developed a University of North Carolina (UNC) food grouping system that aggregates the 4,000 or so foods consumed. This system separates virtually all foods in the USDA's Individual Food Consumption Surveys into 74 useful descriptive and nutrient-based groups. Initially major food groups were based on food groupings used by the USDA. Then fat and dietary fiber compositions were used to develop more refined food groupings, and nutrient thresholds were used to separate major food groups into more distinct, nutrient-based food groups (available from authors on request).

Statistical analysis

Descriptive statistics were generated for each survey year using a commercial software package (SUDAAN version 7.51; Research Triangle Institute, Research Triangle Park, NC) to appropriately correct the standard errors for sample design effects and for applying survey weights. Differences between years in the means of nutrients and servings of the Food Guide Pyramid were then tested for significance in a statistical software program (SAS version 6.12; SAS Institute, Cary, NC) using a Student t test.

PRNewsFoto/Burger King

Staples of the diet of American adolescents do not meet their nutritional needs

Statistical difference was denoted as $P < 0.001$. Nutrient values were compared with those of the most recent recommendations made by the Food and Nutrition Board (recommended dietary allowances [RDA] or recommended dietary intake [RDI]) and expressed as a percentage of the recommendations specific for each age and gender grouping.[20]

RESULTS

Table 1 shows sociodemographic information for the adolescents in the study by survey year. Important trends of interest are the increase in mean household income, the subsequently more even distribution of percentage of households considered below the poverty line starting in 1977, and the increasing number of Hispanics represented in the survey, as well as the increase in body mass index for both younger and older adolescents.

Energy intake decreased over the years, with the greatest drop occurring from 1965 to 1977 (table 2). The data for all 4 years showed typical differences in pattern of energy intake, with boys consuming higher amounts than girls (data not shown). Table 2 also shows the proportion of energy from total fat, saturated fat, carbohydrate, and protein. A steady decline in fats and protein as a proportion of total energy intake occurred in the diet over time, which was compensated by an increase in carbohydrate intake. Gender did not affect the distribution of macro-

Table 1 *Sociodemographic characteristics for adolescents (aged 11-18) with dietary data from the 4 USDA surveys*

Characteristics	1965	1977	1989-1991	1994-1996
No. of individuals	3,061	6,208	1,656	1,573
% of males	51.1	49.4	50.9	50.3
Race (%)*				
White	82.0	76.2	74.9	66.0
Black	15.8	15.8	16.6	16.3
Hispanic	NA	7.1	8.5	12.9
Household size, mean (SEM) no.	5.58 (0.04)	5.22 (0.02)	4.43 (0.03)	4.45 (1.04)
Distribution by region (%)				
Northeast	22.4	23.0	20.3	18.1
North Central	28.7	28.1	24.3	24.8
South	34.4	31.5	36.1	35.2
West	14.5	17.4	19.3	21.9
Distribution by urbanization (%)				
Central city	NA†	27.7	26.8	28.4
Suburban	NA	38.5	47.2	48.8
Rural	35.9	33.8	26.0	22.8
Household income, mean (SEM) $	7,116 (85)	17,517 (159)	40,429 (531)	44,635 (712)
Distribution by percentage of poverty (%)				
<185	56.3	37.0	33.0	37.1
185-350	32.7	38.3	33.6	29.8
>350	11.0	24.8	33.4	33.0
Body mass index (SEM)				
11-14 year olds	19.49 (0.08)	19.89 (0.07)	20.24 (0.13)	20.74 (0.15)
15-18 year olds	21.35 (0.08)	21.40 (0.06)	22.26 (0.15)	22.76 (0.17)

The 4 USDA surveys are the Nationwide Food Consumption Survey, 1965 and 1977, and the Continuing Survey of Food Intake by Individuals, 1989-1991 and 1994-1996. NA = not available.
*USDA began collecting data on Hispanic origin in 1977; the remaining percentage represents other minorities.
†In 1965, USDA coded this variable as urban, rural non-farm, and rural farm. The only comparable variable we could create was rural by adding the 2 rural categories. The other 64% is thus a combination of central city and suburban.

nutrients (data not shown). Between 1989-1991 and 1994-1996, fat intake increased from 80 to 83 g per day, saturated fat intake stayed at 30 g per day, carbohydrate intake increased from 270 to 311 g per day, and protein intake remained relatively unchanged (increased from 81-82 g per day).

Other nutrients of interest that we examined included vitamins A and C, iron, folate, calcium, and fiber. On average, only vitamin A and calcium concentrations decreased, so that in 1996 the mean percentage of the recommended intakes being met for each nutrient was 103% and 74%, respectively. The other 4 nutrient concentrations increased, and concentrations for all but folate and fiber met the most recent dietary recommendations. Some slight differences by gender existed. For example, in 1996, 40% of adolescent girls met the recommended dietary intakes for iron, 20% for calcium, and 17% for folate. For adolescent boys, 75% met the recommendations for iron, and about one third met the recommendations for calcium and folate.

The most interesting trends of food group consumption are shown in figures 1, 2, 3, 4, and 5 by gender and in table 3 for the entire age group (data for other foods are available from the authors on request). The figures reflect the per capita grams of food consumed per day using the UNC food groups. The table presents actual servings of food groups or, as in the case of meat, ounces of lean meat equivalents using the USDA's Food Guide Pyramid database. The results show a decline in milk consumption that was not compensated for by an increase in consuming other dairy products. Low-fat milk was substituted for whole milk (medium-fat source). Grain intake increased but primarily from high-fat mixed dishes such as pizza, macaroni-and-cheese, and certain ethnic foods. Raw fruit consumption declined steadily, but juice consumption increased; this accounts for the relatively stable number of servings in table 3. Figure 4 shows a decrease in the grams of dark green and orange vegetables consumed from 1965 to 1989 and an increase from 1989 to 1996. Since 1965, the grams of high-fat potatoes consumed have increased. By 1996, white potatoes accounted for half of the vegetable consumption, whereas in 1965 it accounted for only a third (table 3). Thus, the overall vegetable consumption has increased since 1965 for this population.

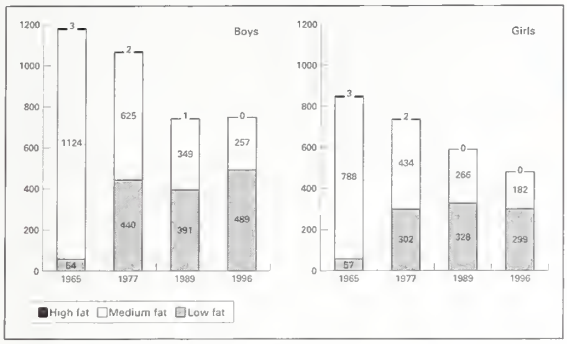

Figure 1 Trends in milk consumption, per capita grams, among US adolescents in the US Department of Agriculture surveys, 1965-1996.

The consumption of lean meat and eggs decreased. Finally, soft drink consumption rose sharply.

DISCUSSION

This is the first study to examine dietary trends among US adolescents that uses actual dietary intake data that are comparable from a nationally representative sample over 3 decades. The small sample size for non-Hispanic African American and Hispanic subgroups forced us to focus on the total adolescent population. Our results show a decrease in total energy intake and total fat over the period studied, the latter of which is positive, but also a decreased consumption of raw fruits, nonpotato sources of vegetables, and calcium-rich dairy sources. Soft drink consumption increased greatly. Many national surveys that focus on adolescents, such as the Youth Risk Behavior Surveillance System (funded by the Centers for Disease Control and Prevention) and the National Longitudinal Survey of Adolescent Health (funded by the National Institutes of Health) lack the appropriate dietary data to quantify these trends.

The total energy intake observed between 1965 and 1996 was below recommendations and decreased with time in each age and gender group. Overall, energy intake declined 17% during this 30-year period. In the last period between 1989-1991 and 1994-1996, mean energy intake increased by 9%. Future surveys need to show if this is a real trend or related to the major methodologic changes between these 2 surveys. Both the NHANES and CSFII reported this increased intake, but both changed their approaches to provide more in-depth probing for dietary intake to avoid some of the undercounting found in the past. The decreased energy intake seems counterintuitive when other studies have shown a rising prevalence of overweight and obesity among adolescents.[8,9,21] The most likely explanation, apart from the 9% increase in total energy intake from 1989 to 1996, is a concomi-

Table 2 *Selected nutrient intakes of 11-18 year olds with 1 day of dietary data from the 4 USDA surveys*

Nutrient	1965	1977	1989-1991	1994-1996
Energy (megajoules)	9.92 (0.16)*†	8.78 (0.09)¶	8.77 (0.18)#	9.58 (0.18)
Total fat, % of energy	38.7 (0.2)*†‡	37 (0.2)§¶	34.3 (0.4)#	32.7 (0.2)
Saturated fat, % of energy	15 (0.1)*†‡	14.1 (0.1)§¶	12.9 (0.2)#	11.6 (0.1)
Carbohydrate, % of energy	46.3 (0.3)†‡	47.1 (0.2)§¶	51.4 (0.5)#	54.2 (0.3)
Protein, % of energy	16.1 (0.1)*	16.7 (0.1)§	15.4 (0.2)#	14.2 (0.1)
Vitamin A (retinol equiv)	1115 (43.1)†‡	1026 (26.8)	902 (33.0)	932 (32.3)
Vitamin C (mg)	89 (2.2)	90 (2.0)	103 (4.1)	105 (4.4)
Iron (mg)	14 (0.2)†	14 (0.2)¶	15 (0.4)#	17 (0.4)
Folate (μg)	244 (4.5)*	265 (4)	272 (7.4)	274 (8.3)
Calcium (mg)	1100 (22.1)*†‡	1009 (15.6)	974 (23.6)	960 (18.6)
Fiber (g)	13.5 (0.3)‡	13 (0.2)¶	14 (0.3)	15 (0.4)

Results expressed as mean (SEM). The 4 USDA surveys are the Nationwide Food Consumption Survey, 1965 and 1977, and the Continuing Survey of Food Intake by Individuals, 1989-1991 and 1994-1996.
*Significant differences between 1965 and 1977, $P < 0.001$.
†Significant differences between 1965 and 1989, $P < 0.001$.
‡Significant differences between 1965 and 1996, $P < 0.001$.
§Significant differences between 1977 and 1989, $P < 0.001$.
¶Significant differences between 1977 and 1996, $P < 0.001$.
#Significant differences between 1989 and 1996, $P < 0.001$.

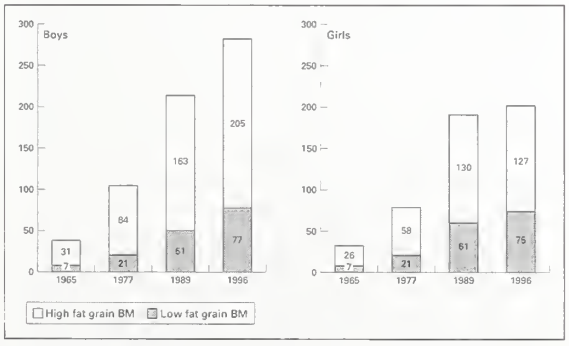

Figure 2 Trends in consumption of grain-based mixed (BM) dishes, by per capita grams, among US adolescents in the US Department of Agriculture surveys, 1965-1996.

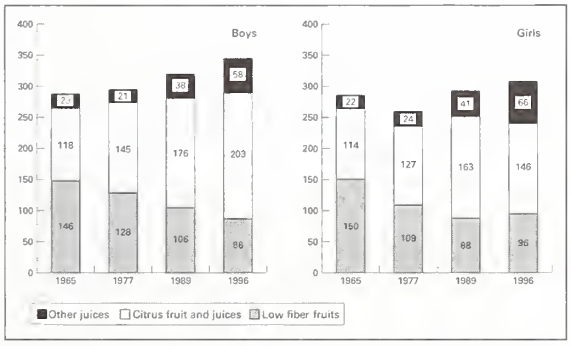

Figure 3 Trends in consumption of raw fruit and juices, by per capita grams, among US adolescents in the US Department of Agriculture surveys, 1965-1996.

Table 3 *Mean Food Guide Pyramid servings of 11-18 years olds with 1 day of dietary data from the 4 USDA surveys*

Food group	1965	1977	1989-1991	1994-1996
Dairy	2.5 (0.07)‡	2.3 (0.05)¶	2.2 (0.07)	2.0 (0.05)
Grain	6.6 (0.12)*‡	6.2 (0.07)§¶	7.1 (0.20)	7.7 (0.11)
Fruit (incl. juices)	1.4 (0.06)	1.1 (0.04)	1.2 (0.07)	1.4 (0.04)
Vegetables (all)	2.7 (0.06)*‡	3.0 (0.06)	3.0 (0.10)#	3.3 (0.07)
White potato	0.8 (0.02)*†‡	1.1 (0.03)¶	1.3 (0.08)	1.5 (0.06)
Meat (ounces)				
Meat, poultry, and fish**	5.6 (0.12)*†‡	5.0 (0.07)§¶	4.0 (0.10)	4.0 (0.09)
Eggs††	0.7 (0.02)*†‡	0.5 (0.01)§¶	0.3 (0.03)	0.3 (0.02)
Nuts and seeds‡‡	0.3 (0.03)*†‡	0.1 (0.01)	0.1 (0.02)	0.2 (0.01)

Results expressed as mean (SEM).
The four USDA surveys are the Nationwide Food Consumption Survey 1965 and 1977, and the Continuing Survey of Food Intake by Individuals 1989-1991 and 1994-1996.
*Significant differences between 1965 and 1977, $P < 0.001$.
†Significant differences between 1965 and 1989, $P < 0.001$.
‡Significant differences between 1965 and 1996, $P < 0.001$.
§Significant differences between 1977 and 1989, $P < 0.001$.
¶Significant differences between 1977 and 1996, $P < 0.001$.
#Significant differences between 1989 and 1996, $P < 0.001$.
**Ounces of cooked lean meat equivalents from beef, pork, veal, lamb, game; frankfurters, sausages, and luncheon meats; poultry; and fish and shellfish.
††One egg is equivalent to 1 oz of cooked lean meat. Includes eggs and egg substitutes.
‡‡One-third cup of nuts and one-fourth cup of seeds is equivalent to 1 oz of cooked lean meat.

tant decrease in energy expenditure caused by a decrease in physical activity.[3] Most children as they age decrease their physical activity.[3,22,23] Another explanation is differential underreporting by year of the survey, with more underreporting occurring in 1996 than in 1965. However, with each survey, the method for collecting the dietary information improved; in the latest survey, more probing and a multipass approach were used to decrease the amount of underreporting.[24] Therefore, more underreporting may have occurred in 1965 than in 1996, which would have led to underestimating the difference in energy intake.

As with older Americans, adolescents still had a higher

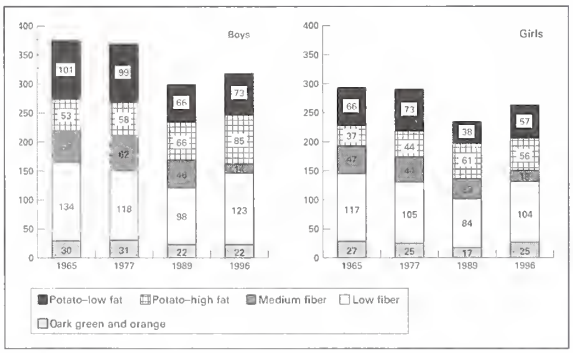

Figure 4 Trends in vegetable consumption, by per capita grams, among US adolescents in the US Department of Agriculture surveys, 1965-1996.

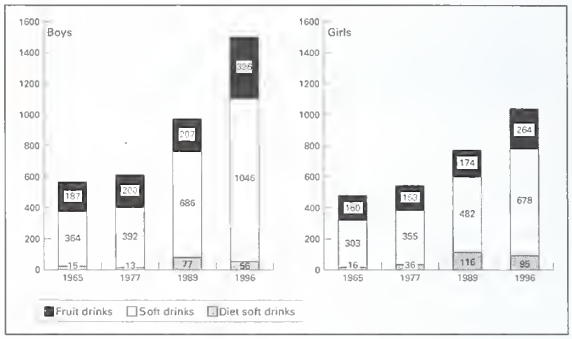

Figure 5 Trends in beverage consumption, by per capita grams, among US adolescents in the US Department of Agriculture surveys, 1965-1996.

percentage of energy intake from fat than the current dietary guidelines recommend.[25,26] The proportion of energy coming from carbohydrate and protein was within recommendations. In terms of the absolute intake of food, however, we found that between 1989 and 1996, total fat intake increased by 4%, saturated fat intake remained stable, carbohydrate intake increased by 15%, and protein intake increased by 1%. Intakes of fiber (the recommendation being more than 10 g per 4.18 megajoules),[27] folic acid, and calcium for the entire age group and iron for girls were lower than optimum for proper growth and development during adolescence.

Several of these trends combined create important nutritional problems. Inadequate fiber consumption and decreasing consumption of raw fruit and nonpotato vegetables are major concerns. Others in the field have substantiated these findings for this age group and for younger ages.[28,29] Adolescents do not consume other sources of fiber, such as whole grains, pasta, rice, bread, and high-fiber cereals, in sufficient quantities to make a difference in the total fiber intake. Thus, they are at risk of chronic diseases because of low intake of not only fiber but also of antioxidant and nutrient sources of plant foods that may serve as protective factors for certain cancers.[14]

Another example of a potential nutritional problem is the decreased consumption of milk, which has not been replaced by other rich sources of calcium but rather by soft drinks and noncitrus juices and drinks. Both adolescent boys and girls have decreased their milk consumption, but this is of greater concern for girls, who may be at a higher risk for developing osteoporosis later in life. Adolescence is the optimal period to increase bone density.[2] This trend, coupled with the low consumption of dark green and orange vegetables among adolescents, may be more problematic than once thought. Preliminary findings suggest that this dietary behavior leads to increased phosphorus excretion, which subsequently may compromise bone building and maintenance.[30] All age groups are susceptible to dental caries and hyperlipidemia, 2 nutritional

consequences of increased simple carbohydrate intake generated by increased soft drink consumption.[31]

Another area of concern is the low intake of dietary folate and iron for adolescent girls. If adolescents with low intakes become pregnant, their risks of iron deficiency anemia and of having an infant with neural tube defects are increased. More nutrition intervention strategies are needed to improve the intakes of these nutrients. Recommending increased supplement use and fortification are key options.

CONCLUSION

Food consumption trends are compromising the nutrition and health of US adolescents and may contribute to important increases in nutrition-related chronic diseases. Given our increasing understanding of the role that diet and body composition play in preventing disease and promoting a higher quality of life, these results provide a clearer basis for intervention during adolescence to instill proper dietary habits.

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COMMENTARY

Clinical implications of trends in food intake among US adolescents

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The accompanying research article by Cavadini and colleagues raises many concerns over the eating patterns of US adolescents and the possible long-term health implications of these behaviors. Analyzing data collected from 1965 through 1996 as part of the Continuing Survey of Food Intakes by Individuals (CSFII), the authors found some disturbing trends in eating patterns and weight status of teens, including a substantial increase in body mass index (BMI). Other national surveys, including the National Health and Nutrition Examination Survey (NHANES), have also shown a temporal increase in body mass index (BMI).[1] According to new guidelines on the detection and treatment of overweight among youth, a BMI value that is equal to or greater than the 85th percentile, but less than the 95th percentile, classifies a teenager as at-risk for overweight, while a BMI value equal to or greater than the 95th percentile classifies a teen as overweight.[2] Using these guidelines, the prevalence of overweight among US adolescents has more than doubled since 1965.[3]

The exact reasons for this dramatic increase in overweight among US youth are not known. Genetic factors alone cannot account for such a striking increase in obesity in such a relatively short time span. Environmental factors have been suggested, such as an increase in energy and/or fat consumption, but the data reported by Cavadini and colleagues only partially support this hypothesis. The intake of both energy and total fat among US adolescents appears to have declined from 1965 to 1989, after which time they began to increase. These relative changes in calorie and fat consumption are not, however, consistent with the increases in BMI. Clearly, other factors must be involved—such as a decrease in energy expenditure secondary to a decrease in physical activity and a change in the overall composition of the dietary intake.

Cavadini and colleagues reported a dramatic increase in the consumption of carbonated beverages accompanied by a reduction in the consumption of fluid milk. Harnack and colleagues, also using CSFII data, reported that carbonated beverages replace milk in the diets of adolescents, thus increasing the intake of sugar and other caloric sweeteners and reducing the nutrient density of the diet.[4] In fact, national data suggest that sweeteners and added sugars alone provide more than 16% of the total calories and 12% of total carbohydrate consumed by US adolescents.[5] This is particularly alarming in light of recent increases in BMI values and the prevalence of overweight among adolescents.[1,3]

Another concern raised by the increase in carbonated beverage consumption accompanied by the decrease in fluid milk consumption is the resulting reduction of intakes of calcium and vitamin D. Calcium intake among adolescents is suboptimal. Stang and colleagues, also using data from the CSFII, showed that as many as two-thirds of US adolescents do not consume at least 75% of the Daily Recommended Intake or Recommended Daily Allowances for calcium.[6] This trend is more pronounced among female teens. The long-term implications of reduced intakes of calcium and vitamin D may include a reduction in peak bone mass and a concomitant increased risk of osteoporosis.

Recent data suggest that the consumption of carbonated beverages increases an adolescent's lifetime risk of bone fractures, particularly among physically active females.[7] A disconcerting clinical situation is imaginable among young and middle-aged adults: their chronic long-term consumption of carbonated beverages leads to a greatly reduced peak bone mass, compounded by obesity which causes them to carry excessive weight and prevents them from participating in moderate to strenuous physical activity. Certainly, the optimal time for intervention related to improving dietary intake and maintaining a healthy body weight is during childhood and adolescence.

The Guidelines for Adolescent Preventive Services suggest that annual screening and education be provided to adolescents around the issues of eating a healthy diet and maintaining a healthy weight.[8] The study by Cavadini and colleagues clearly illustrates the need for providing routine anticipatory guidance to children, adolescents, and their families with regard to eating and physical activity behaviors. *Bright Futures in Practice: Nutrition,*[9] and the soon-to-be-released *Bright Futures in Practice: Physical Activity,* provide guidelines for developmentally appropriate anticipatory guidance on these topics that can be implemented in clinical settings.

Jamie Stang directs a program that provides graduate and post-doctoral level training, continuing education, and technical assistance in the area of maternal and child nutrition.

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Qualitative interview study of communication between parents and children about maternal breast cancer

ABSTRACT **Objective** To examine parents' communication with their children about the diagnosis and initial treatment of breast cancer in the mother. **Design** Qualitative interview study within a cross-sectional cohort. **Setting** Two breast cancer treatment centers. **Participants** 32 women with stage I or stage II breast cancer with 56 school-aged children. **Main outcome measures** Semistructured interview regarding timing and extent of communication with children about the diagnosis and initial treatment of the mother's illness, reasons for talking to children or withholding information, and help available and requested from health professionals. **Results** Women were most likely to begin talking to their children after their diagnosis had been confirmed by biopsy, but a few waited until after surgery or said nothing at all. Family discussion did not necessarily include mention of cancer. There was considerable consistency in the reasons given for either discussing or not discussing the diagnosis. The most common reason for not communicating was to avoid children's questions, particularly those about death. Although most women had helpful discussion with a physician concerning their illness, few were offered help with talking to their children; many would have liked help, particularly the opportunity for both parents to talk to a health professional with experience in understanding and talking to children. **Conclusion** Parents diagnosed with cancer or other serious illnesses should be offered help to think about whether, what, and how to tell their children and about what children can understand, especially as they may well be struggling themselves to come to terms with their illness.

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INTRODUCTION

In the past 10 years, there has been increased acknowledgment of the importance of physicians' communication with patients concerning the diagnosis of cancer. An editorial in the *BMJ* highlighted the difficulties many physicians have in communicating such news.[1] If it is difficult for physicians, however, it is likely to be even more difficult for parents with newly diagnosed cancer to tell their children while dealing with their own feelings and coming to terms with the implications themselves.[2]

There is evidence that good doctor-patient communication about the diagnosis and shared decision making about treatment are important and have a protective effect on patients' psychological adjustment.[3] Little attention, however, has been paid to whether, what, and how children should be told about their parent's diagnosis. This responsibility has been left largely to parents.

The little research that has been conducted on this issue suggests that when children are told of the diagnosis, their anxiety levels are lower and communication within the family is improved,[4] although factors such as the child's age have not been studied in detail. In addition, a large study in the United States has shown that in families where the mother has cancer, parents are often not aware of the extent of psychological symptoms and distress of their children.[5] No study to date has examined the timing, nature, and extent of communication between parents with cancer and their children or why parents do or do not talk to their children about such difficult and important issues or inquired about what help parents have received or might have liked.

The relative frequency of life-threatening illness in general among parents makes the issue of communication with their children an important public health matter.

Breast cancer affects 1 in 12 women in the United Kingdom, about 30% of whom are likely to be diagnosed while they have children of school age living at home.[6] Therefore, families in which the mother has recently been diagnosed as having breast cancer are a particularly important group for study of the communication of the diagnosis to the children. We examined the nature of such communication, established whether parents were given any support or advice concerning the communication, and identified what support or guidance they might have wanted.

METHODS

Recruitment

A consecutive series of women was approached at 2 breast cancer treatment clinics in north London hospitals over about 18 months. Those with stage I or stage II breast cancer (about 80% of patients) and who had at least 1 child aged between 5 and 18 years were approached by the breast surgeon or oncologist in outpatient clinics between 4 and 6 months after diagnosis. The women were given information and a consent form, and if interested, they contacted the research team. Approval was obtained from 2 local research ethics committees. Full informed consent was obtained, and it was explained that participation would not influence their ongoing medical care.

Thirty-two women who fulfilled the criteria completed the study. Five women expressed interest but dropped out, and 16 who were approached did not make contact. A further 15 were interviewed but fell outside the study criteria, either because of characteristics of their illness or their children's ages. Their data are not presented in this article. Interviews were conducted either in the home or in a research office. The mean (range) age of the 32 women who fulfilled criteria and were interviewed was 43 (31-52) years. In total, they had 56 children (35 boys) with a mean age of 12 years. Fourteen women had 1 child, 12 had 2, and 6 had 3. Most (27) were married or in a stable relationship; their socioeconomic status was classified according to the mother's occupation, unless she had never been employed (8 were professional, 14 were managerial, 6 were clerical, and 4 were manual); with a range of educational qualifications (10 had a college degree; 9 had A levels [that is, associate-level degrees]; 10 had General Certificates of Education [equivalent to high school diploma], and 3 had none [equivalent to not completing high school]). There was a bias toward middle-class occupations, reflecting in part the population of the community. The number of children per family was evenly distributed in relation to maternal educational qualifications and social class.

Summary points

- Retrospective studies report that many children are not told when a parent has a severe, life-threatening illness
- Communication between parents and children may reduce children's anxiety
- Parents were most likely to initiate communication once a definite diagnosis was made, but many withheld the fact that their illness was cancer
- Women gave clear reasons both for communicating and not communicating with their children
- A particular concern was about dealing with children's questions and comments about death
- Many women would have liked to consult a health professional with experience in child development, preferably with both parents or as a family

Trevillion Picture Library

Both parents and children need support when facing serious illness

Outcome measures

A semistructured interview incorporated certain questions from established instruments[7,8] and was designed for this study to elicit both quantitative and qualitative information. Only the qualitative information is presented in this article. The interview covered sociodemographic data, followed by a combination of structured (yes/no) and open-ended questions about the history of illness and treatment, communication with children and other family members and friends at specific times during the illness, children's understanding of the illness and treatment, and any emotional or behavioral problems in the children. Women were asked about their children's questions, reactions, and concerns. Although the interviewer had a number of topics to cover, interviews were conducted in a manner that was sensitive to the interviewee and her narrative, allowing for promptings and exploration of topics raised spontaneously, to enhance the qualitative information elicited.[9] All interviews were tape recorded and transcribed.

Transcripts were scrutinized by 3 members of the research team (J B, L K, and J L), who analyzed them using content analysis.[10] The research group made lists of initial themes under broad headings (for example, reasons for talking or not talking to children, and ways to help), and the additional major themes were identified on the basis of the interviews (for example, the questions children ask, what is the meaning of cancer, and children's understanding of death). Transcripts were read again and passages relating to each theme collected together. Agreement was established among the 3 coders on the text applying to the initial themes by using the first 10 transcripts. Each further transcript was read by at least 2 members of the team to identify relevant content and any additional themes.

RESULTS

Timing of disclosure to children

Whereas nearly all women interviewed had talked to their partners from the early stages (22/29 at discovery of the lump, 20/26 at visit to the general practitioner, and 28/29 at outpatient appointment), few women told their children at that time. For women who decided to share information about their illness, children were usually told at the time of diagnosis (39/56), but there was considerable variation in the extent to which children were told about the nature and possible consequences of the illness. At the stage of surgery, 44 children had been told that their mother was ill but only 32 that her illness was cancer.

Reasons for disclosure or nondisclosure

The qualitative analysis was designed to explore women's decisions about making disclosures regarding their illness (see first box). There was considerable consistency in the reasons given for either discussing or not discussing the diagnosis with their children. The most common reason for not discussing the diagnosis was to avoid facing children's questions and, in particular, those concerned with death. Women also talked about protecting their children by preventing anxiety and distress, which they expected to come from children's knowledge of their illness. Discussion was also avoided because children's understanding of the illness was not expected or to preserve special family occasions such as holidays. Those women who had communicated in detail with their children at an early stage in their illness and often with details of the nature of cancer said that they thought children had a right to know (see second box). They also said that they wanted to keep their children's trust and to promote discussion in the family, which they hoped would alleviate children's anxieties

Reasons for wanting to withhold information from children

- **To avoid facing questions about cancer and death**

  I think, I'm not just talking about children, I'm talking about anybody; you mention cancer to anybody, and you're dead in front of them (mother of 8-year-old)

  In the past, she has said, "What's cancer?" And I've said, "It's something that people die of," and I feel that if I mentioned it to her, she would just worry so much (mother of 7-year-old)

  He'll say, "Just a minute, Mummy, you've got cancer; are you going to die?" (mother of 9-year-old)

- **To prevent children's distress**

  I thought she would think after the mastectomy that I'm someone different or visualize something really horrific. That's what made me hold back (mother of 10-year-old)

  He basically said he didn't want to talk about it because it made him too upset (mother of 12-year-old)

  I feel that if I mentioned it to him, he would just worry so much (mother of 7-year-old)

- **Children's understanding is not expected**

  He knows that people can get sick and people can die and not come back, but he's more likely to think that you'll die by drowning or getting run over by a bus than to actually fade away with an illness. For him, the word "cancer" wouldn't have the same impact (mother of 6-year-old)

  He asked me why I'd gone to the doctor's, so I said because I'd got a lump in my breast and I wanted the doctor to have a look, and he said, "Have you got breast cancer? Will they cut it off? Will you die?" I was extremely taken aback that he had all that in his head about the implications of having a lump (mother of 10-year-old)

- **To preserve special family times**

  I was thinking, I don't want her to be worried over Christmas. I don't want this Christmas to be any different from all the other lovely Christmases we've had (mother of 16-year-old)

about their mother's changed appearance or the possibility of death.

Ways to help parents think about communication with their children

Women were asked whether they had been offered any help with talking to their children from a list of possible services and supports. Although they had received careful discussion concerning the diagnosis and treatment of their illness, only a minority had been offered any kind of help with regard to communicating the information to their children, thinking about their children's reactions, or about the issues surrounding talking to children about serious illness. Many would have liked a meeting as parents, or as a whole family, with a health professional, preferably in their own home (see third box). Specifically, they would have liked advice on ways to break news to their children based on detailed knowledge of child development. They also thought their children might benefit from talking directly to a health care professional, such as a nurse or the surgeon.

Women explained in their spontaneous comments that they wanted information about the most appropriate language to use with children. They felt unsure about their children's understanding of illness and death and wanted guidance on ways to communicate effectively. They also wanted to familiarize their children with the medical environment and to have more amenities available for children when the women attended appointments.

Reasons for wanting children to have information

- **Belief in communicating**

  We needed to be able to talk about how we felt about everything that had happened (mother of 12- and 10-year-olds)

  Sooner or later, they were going to know. Why not tell them straight away? I tell them frankly what is happening. I think they find it much easier to cope because they are ready for things (mother of 16-, 13-, and 12-year-olds)

- **Desire to keep children's trust**

  You have got to be open with them. If you hide it, and then you tell them after a few years, they would resent it (mother of 15-, 13-, and 12-year-olds)

  We mustn't just brush them away. Children are aware, and children can cope, so I've never pretended with him, but I certainly accentuate the positive (mother of 5-year-old)

- **Communication expected to alleviate children's distress**

  You could see the relief in her face when I said, "Oh, the doctor said what I've got is curable, but I have to have treatment, and my hair is going to fall off" (mother of 10-year-old)

  It is probably better to tell them straight away than leave it for a long delay. If you don't say anything, it's worse for kids, especially as I was edgy. They can sense that something is wrong (mother of 15- and 13-year-olds)

Help and facilities that women would have liked

- **Knowledge of child development and age-appropriate strategies**

  Talking to somebody who knew how the child interpreted things would be helpful because I was always of the opinion that he's far too young to understand, but the more you sit down and think about it, I could have said more to him (mother of 6-year-old)

  I would have liked some counseling as to how you break such shattering news to a 5-year-old (mother of 5-year-old)

  It would have been nice to have had the names of books about how to talk to children then [at diagnosis], even if we weren't in a state to listen to advice about how to break the news to the children (mother of 8-year-old)

- **Space and consideration for children in the hospital**

  If there was any sort of crèche facility [that is, drop-in child care], it would have made a huge difference (mother of 5-year-old)

  The time I brought my son here, there was nowhere else to go, and he might not have necessarily been adequately prepared to see all these gadgets attached to his mother (mother of 8-year-old boy)

- **Preparation for the experience**

  I would have liked her to come with me one time, when I was seeing the surgeon or maybe after, just to be in the hospital and see it wasn't in any way a threatening or frightening experience (mother of 18-year-old)

  A place that kids could come together in a group and talk, to share their feelings, and make friends with them. They could say to each other, "Well, my Mum's had that as well" (mother of 15- and 12-year-old boys)

DISCUSSION

Children are keen observers of their environment, and studies of family disruptions such as divorce have shown that they construct meaning for themselves, even blaming themselves for the ensuing changes.[11] Women faced with a potentially life-threatening illness may decide not to talk to their children about their condition. Our study has shown that some are reluctant to reveal their illness even after surgery. The results suggest that, in general, parents avoid communication with their children as a means of filtering information in the hope of controlling or minimizing the children's difficulties.

There was a striking consistency in the spontaneous comments from women about why they did, or did not, discuss their illness. In many cases, parents hoped to re-

duce the distress for their children and for themselves, and in particular, they wanted to avoid mention of death. In addition, the extent of discussions was influenced by parents being unclear what children could understand, how they would react, and how to cope and respond when questions were asked.

Children are now known to have more potential to understand complex concepts of illness than many professionals had previously thought.[12] Even if children are not told of the illness, they soon become aware of changes in the atmosphere at home and in their parent's health. Parents receiving a diagnosis of cancer need to be offered support and acknowledgment that they are part of a family unit, all the members of which are likely to be profoundly affected by the illness and its treatment. Many parents need help to think about how they might talk to their children about the diagnosis and changes in family life. They are likely to benefit from discussion, even if they decide not to communicate any details to their children. Such advice should take into account children's ages, the family's communication style, and the parent's feelings about his or her illness and capacity to cope with their children's feelings and reactions.

More research is needed to investigate the best means of providing support and the consequences for the parents and children of more or less communication. Knowledge of ways that families respond to illness should have implications for undergraduate and postgraduate medical and nursing training. It will also have applications in other situations of loss and distress, such as coping with chronic physical illness in a parent or severe injuries resulting from motor vehicle accidents.

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COMMENTARY

Treating cancer as a family disease

Cancer affects both the individual and his or her collective social network. Like other serious illnesses, it changes lives by changing people's psychology, their life span, and their quality of life. In an attempt to control and minimize this effect, people sometimes avoid talking about cancer. Instead, they whisper about it, talk behind closed doors, or keep feelings locked away.

Time has changed our willingness to talk about cancer. In the not-too-distant past, speaking to patients about their diagnosis was considered unacceptable. Adult family members would be told, and patients would be denied the opportunity to make choices, hear information, confront their fears, and personally grow from the experience. But research findings have altered our practice, and patients are now included as part of the treatment team. Young children are also involved in the process, and Barnes and colleagues' article articulates how a few families have dealt with a diagnosis of breast cancer.

Their qualitative study describes the decisions that parents make about whether to share a breast cancer diagnosis with their children. It explores why they do so and—most important—their unmet needs for support in the sharing process. The study alerts us to an absence of information and resources to help parents.

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One of the characteristic experiences of the cancer "journey" is the initial feeling of being alone. This comes from people walking into an unknown territory without companionship. Physicians, the medical team, and mental health professionals play a vital role in providing the companionship and guidance that patients need to feel less alone and, therefore, less afraid. A doctor-patient relationship, like a parent-child relationship, is built on trust, and both need open and honest communication. So what can a primary care physician do to assist patients and help them feel less alone regarding children?

- Recognize psychosocial need on an ongoing basis

Ask all patients, both adults and children, about their concerns. They may wish to share their concerns with other patients who have a similar diagnosis.

- Make psychosocial referrals

Not all physicians can know the appropriate literature or all the resources available for patients, but they can know who has the expertise and make referrals. Too often referrals are made to mental health professionals only when there is an "identified problem." All patients have concerns, and mental health professionals—such as oncology counselors, social workers, and health psychologists—can help to provide companionship, information, reassurance, and assistance with problem solving.

- Suggest a family meeting

Patients may not feel comfortable asking their physicians to help them communicate with their children. But by offering to have a family meeting, physicians can build trust and encourage parents to talk to children. This helps treat cancer as a family disease and promotes trust and well-being for the entire family.

- Refer patients to appropriate reading materials

Suitable materials for children and parents are shown in the list of resources.

Illness is not something that anyone chooses in their life. However, it can lead to deeper connections and more meaningful relationships for those touched and changed by it—regardless of their age, profession, or role in life—and physicians can help in this process.

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Resources: useful books for parents and children

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A survey of physician attitudes and practices concerning cost-effectiveness in patient care

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ABSTRACT **Objective** To identify physicians' views regarding cost-containment and cost-effectiveness and their attitudes and experience using cost-effectiveness in clinical decision making. **Design** A close-ended 30-item written survey. **Subjects** 1,000 randomly selected physicians whose practices currently encompass direct patient care and who work in the California counties of Sacramento, Yolo, Placer, Nevada, and El Dorado. **Outcome measures** Physician attitudes about the role of cost and cost-effectiveness in treatment decisions, perceived barriers to cost-effective medical practice, and response of physicians and patients if there are conflicts about treatment that physicians consider either not indicated or not cost-effective. **Results** Most physicians regard cost-effectiveness as an appropriate component of clinical decisions and think that only the treating physician and patient should decide what is cost-worthy. However, physicians are divided on whether they have a duty to offer medical interventions with remote chances of benefit regardless of cost, and they vary considerably in their interactions with patients when cost-effectiveness is an issue. **Conclusion** Although physicians in the Sacramento region accept cost-effectiveness as important and appropriate in clinical practice, there is little uniformity in how cost-effectiveness decisions are implemented.

The rising cost and the equitable distribution of health care resources are important social and political issues. A major contributor to cost inflation is the enormous capacity of biomedical science to create new and costly medical interventions.[1,2] Whereas purchasers—primarily employers and government—resist increases in health care premiums and reimbursements, physicians, medical groups, and health plans face legal, regulatory, and social pressures to provide all care that is "medically necessary."[3,4]

Reconciling the tension between finite resources and ever-increasing demands is not easy. One approach is for physicians to use cost-effectiveness as an explicit criterion when developing clinical policies applicable to broad populations or when considering treatment alternatives for individual patients.[5,6] Although using cost-effectiveness criteria to develop clinical policies (eg, drug formularies or practice guidelines) has long been considered an appropriate physician role,[7,8] limiting marginally beneficial and costly interventions for individual patients is controversial.[9-13] The literature on the cost-effectiveness of medical interventions is growing, but little is known about how physicians incorporate cost-effectiveness decisions at the bedside.

To explore the acceptability of explicitly incorporating cost-effectiveness into clinical and coverage decisions, a regional 15-member consortium (listed at the end of article) created the Visible Fairness project. Its goal is to develop recommendations that reflect consumer and provider values, interests, and concerns regarding cost-effectiveness. The first component of Visible Fairness was a written survey of local physicians seeking their views on 3 principal issues: cost containment and the role of physicians in providing cost-effective care, barriers to practicing cost-effective medicine, and experience with patients who insist on treatment that is viewed as not cost-effective.

METHODS

The 30-item survey, titled Cost-Effectiveness in Medical Practice, was designed in spring 2000 by Visible Fairness members, staff, and consultants. The following definition preceded the questions: For the purpose of this survey, a medical intervention (eg, a diagnostic test, procedure, treatment, or pharmaceutical) is cost-effective when, for example, the intervention achieves a benefit comparable to an alternative intervention but at a lower cost; or the intervention achieves a greater benefit than an alternative, and the added clinical benefit is worth the additional cost.

Survey sampling

The Sacramento-El Dorado Medical Society provided demographic and professional data on all 3,200 identifiable physicians in the 5-county region of California. The target group was physicians who practice in Sacramento, Yolo, Placer, Nevada, and El Dorado counties and whose primary role is direct patient care. Consequently, we excluded retired physicians, administrative physicians, pathologists, anesthesiologists, and radiologists, reducing the pool to 2,478 physicians. One thousand were then selected through systematic random sampling, a standard process of picking random names from an alphabetized list, ensuring that the entire list had an equal chance of being picked.

Main measures

Questions used to generate the data for this study were organized into 3 sections. The first addressed physicians' attitudes and beliefs about the role of cost containment and cost-effectiveness using 7 Likert-type items (from "strongly agree" to "strongly disagree"). The second section asked physicians to rate the importance of 9 possible barriers to cost-effective practice. The third section included several questions about the physician's experience with patients who insist on having a medical intervention that the physician considers either not indicated or not cost-effective.

Survey administration

The survey was administered by Sacramento Healthcare Decisions, a nonprofit, independent organization that facilitates collaboration on health care issues between consumers and health care providers. The initial survey was mailed June 5, 2000, accompanied by a cover letter explaining its purpose, the sponsoring organizations, the funding agency, and the confidentiality of individual respondents, as well as a $2 gratuity and a self-addressed stamped envelope. A follow-up letter was mailed 2 weeks later to nonrespondents. Of the 1,000 surveys mailed, 11 were returned as undeliverable, 15 were substantially incomplete and not usable, and 18 arrived after the cutoff date of July 15. Of the 989 deliverable surveys, 512 were returned and usable, a 52% response rate. The demographics of respondents—age, sex, and type of practice—were similar to those of nonrespondents. However, survey respondents were more likely than nonrespondents (53% vs 42%) to be affiliated with 1 of the region's 4 large physician-hospital organizations, suggesting that physicians in solo or small group practice were underrepresented. In presenting our results, we did not use inferential statistics or calculate *P* values because we are making inferences only to the sample of physicians who actually completed our survey. Some physicians did not respond to all questions.

RESULTS

Attitudes about cost-effectiveness

Physicians agreed that there is a legitimate need for cost containment and that individual physicians should help in

Summary points

- Although cost-effectiveness has an accepted role in broad clinical policies, little is known about how physicians incorporate it into decisions at the bedside
- Physicians regard cost-effectiveness as an appropriate criterion when making treatment decisions for their patients
- Physicians appear divided on whether they have a duty to offer all treatment options when the chance of success is small and the cost is great
- Despite their support for cost-effectiveness in theory, physicians appear inconsistent in how they apply it in practice
- If cost-effectiveness is to be used as a visible criterion in patient decisions, physicians, consumers, and other stakeholders need to develop consensus on process and communication issues

containing costs (table 1). Seventy-two percent (371 of 512) felt that "it is inappropriate for anyone other than the treating physician and patient to decide if a treatment is worth the cost," suggesting resistance to the intrusion of others in these decisions. Whereas 447 of 512 (88%) thought physicians should consider cost-effectiveness when weighing different medical interventions for their patients, and 425 of 512 (84%) were comfortable with clinical practice guidelines that took account of cost, 271 of 512 (53%) agreed, nevertheless, that "if a medical intervention has any chance of helping the patient, it is the physician's duty to offer it."

Perceived barriers to cost-effective practice

Most respondents viewed all 9 issues as contributing "a great deal" or "somewhat" to difficulties in practicing cost-effective medicine (table 2). The most strongly affirmed barriers were societal issues: "society unwilling to acknowledge limited resources" (336 of 512 [66%] thought it contributed a great deal) and "patients with unrealistic expectations of medicine" (317 of 512 [62%] a great deal). On the other hand, physicians were less ready to blame themselves (of the possible barrier "physicians unaware of costs of medical interventions," 122 of 512 (24%) answered "a great deal"; and of "physicians unwilling to refuse patients' demands," 104 of 512 (21%) answered "a great deal") than they were to blame external factors such as direct-to-consumer advertising and lack of cost-sharing by patients.

Medical decision making and discussions with patients

Almost all physicians reported encounters with patients who insist on having unnecessary or cost-ineffective medical interventions: 272 of 512 (54%) "occasionally," 167 of 512 (33%) "several times a week," and 46 of 512 (9%) "several times daily" (data not shown in tabular form). On average, physicians "try to explain why the intervention is not appropriate and do not order it, even if the patient insists" 56% of the time; they try to "explain why the intervention is not appropriate but order it anyway, if the patient continues to insist" 34% of the time; and they "do not try to talk the patient out of the intervention and will order it anyway, unless it will do the patient harm" 7% of the time (3% of the time they employ other strategies). Classified on the basis of their responses, 232 of 471 (49%) of physicians usually (2/3 of the time) provided an explanation and did not order the requested intervention, 95 of 471 (20%) usually ordered the intervention if pa-

Table 1 *Physician attitudes about cost-containment**

Do you agree or disagree with the following? (n = 512)	Agree strongly	Agree somewhat	Disagree somewhat	Disagree strongly
There is a legitimate need for cost containment in today's health care environment	288 (56)	186 (36)	28 (5)	9 (2)
As individual clinicians, physicians should play a role in helping to control health care costs	313 (61)	174 (34)	18 (4)	7 (1)
It is inappropriate for anyone other than the treating physician and patient to decide if a treatment is "worth the cost"	215 (42)	156 (30)	116 (23)	25 (5)
If a medical intervention has any chance (no matter how small) of helping the patient, it is the physician's duty to offer it regardless of cost	118 (23)	153 (30)	149 (29)	88 (17)
The only time the cost of a medical intervention should be considered is when the patient must pay all or most of the cost	25 (5)	48 (9)	155 (30)	281 (55)
It is appropriate that clinical practice guidelines include cost-effectiveness as a criterion	150 (29)	274 (54)	50 (10)	35 (7)
It is appropriate that physicians consider cost-effectiveness when weighing different medical interventions for their patients	208 (41)	239 (47)	47 (9)	16 (3)

*Data are given as the number of physicians responding, with percentage in parentheses.

tients insisted, and 144 of 471 (31%) employed mixed strategies.

Physicians varied considerably in the frequency with which they referred to cost or cost-effectiveness when talking with patients. Thirty percent reported that they frequently or always mentioned cost or cost-effectiveness when explaining why a treatment is not appropriate, and 21% of physicians said they never do. On average, physicians reported that 45% of patients get "angry or upset if cost or cost-effectiveness is mentioned," and 49% of patients accept explanations that incorporate costs "once they understand that the intervention would waste resources."

DISCUSSION

Principal findings

If cost-effectiveness has the potential for addressing issues of equity and fiscal responsibility, it must be understood and accepted by physicians, patients, and other health care stakeholders. This survey provides new data on physicians' views of the issue. There are several important observations from the survey results.

First, although physicians accept the legitimacy of cost-effectiveness within their medical practice, when and how they consider cost in managing their patients vary considerably. Although most think that only the physician and patient should decide if a treatment is "worth the cost," more than half also think that the physician has a duty to offer any intervention with a chance of benefit, regardless of cost. In addition, many, if pressed, will provide an intervention even when they think it is not indicated or not cost-effective. In sum, physicians accept cost-effectiveness as an appropriate criterion for decision making, but many appear inconsistent in its application or hesitant to apply it in practice.

Second, variations in attitudes extend to communication with patients. Although physicians think that patients' unrealistic expectations are a major barrier to practicing cost-effective medicine, 339 of 483 (70%) infrequently or never discuss cost or cost-effectiveness when it is relevant to decision making. Their reluctance to address this directly with patients may be due to physician discomfort with incorporating costs into treatment decisions, limited time for discussions, or concern about patient reactions—such as the 45% of patients who physicians report becoming angry or upset if cost or cost-effectiveness is mentioned.

Finally, because physicians vary considerably in their willingness to provide care they judge to be cost-ineffective or inappropriate, inconsistencies in patient care are inevitable. Similar patients may not receive similar care, depending on their physician's views on cost-effectiveness. At a time when many patients appear to mistrust the health care system, such inequities—perceived or real—could exacerbate already strained relationships.

Limitations of the study

The results of this survey must be interpreted in light of its limitations: the survey definition of cost-effectiveness was not all-inclusive, the nonresponders (477 of 989 [48%]) might have answered differently, Likert scales can capture only broad perspectives, complex issues do not easily compress into simple answers, and what physicians say may differ from what they do. In addition, this survey does not assess the reasons for variations in physicians' responses,

Table 2 *Perceived barriers to cost-effective practice**

	Contributes to the difficulty			
	A great deal	Somewhat	A little	Not at all
Inadequate information on the cost-effectivelness of medical interventions	204 (40)	231 (46)	63 (12)	7 (1)
Patients with unrealistic expectations of what medicine can do	317 (62)	160 (31)	28 (6)	3 (1)
Coverage decisions that consider only the short-term benefits for patients but not the long-term benefits	203 (41)	225 (45)	55 (11)	17 (3)
Patients not directly sharing the cost of their health care interventions	217 (43)	211 (42)	61 (12)	17 (3)
Society unwilling to acknowledge limits to health care resources	336 (66)	135 (27)	28 (6)	7 (1)
Physicians being unaware of the cost of medical interventions	122 (24)	252 (50)	109 (22)	23 (5)
The need to practice defensive medicine	195 (39)	230 (46)	72 (14)	7 (1)
Direct-to-consumer advertising about drugs and treatment	222 (44)	193 (38)	78 (15)	14 (3)
Physicians unwilling to refuse patients' demands for unnecessary interventions	104 (21)	268 (53)	112 (22)	22 (4)

*Data are given as the number of physicians responding, with percentage in parentheses.

such as the cost of interventions being considered, the severity of medical problems, or the payer source.

Implications of the study

Despite the limitations, the survey results provide a sound basis for initiating a public dialogue. Is the public willing to accept cost-effectiveness as a treatment criterion? If so, what role does it want physicians to play? Should physicians discuss cost-effectiveness with patients when it is a factor in decision making? How can discussions lead to understanding rather than patient anger? Does the public prefer a system with general rules about what services will or will not be provided—a system perhaps more consistent but less sensitive to the particularities of individual cases?

Future research

The next phase of Visible Fairness will be to pursue answers to these questions with community-based focus groups. In 2001, Visible Fairness will reconvene physicians and consumers for more in-depth discussion of cost-effectiveness in making patient care decisions.

Visible Fairness partner organizations (representative in parentheses): American Association of Retired Persons (Stephanie Zack); CalPERS (Nancy Welsh); Fred Simmons Insurance (Fred Simmons); Health Net (Steven Raffin); Health Rights Hotline (Shelley Rouillard); Kaiser Foundation Health Plan (Edward S Glavis); Mary J Griffin & Associates (Mary Griffin); MedClinic/Mercy Healthcare Sacramento (Jennifer Nuovo); Sacramento-El Dorado Medical Society (William A Sandberg); Sacramento Healthcare Decisions (Marjorie Ginsburg); San Juan School District (Charles Diggs); Sutter Medical Group (Gary Fields); The Permanente Medical Group (Jack Rozance); University of California, Davis, Health System (Robert Chason); and Western Health Advantage (Donald Hufford).

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COMMENTARY

Cost-effectiveness: no easy choices or answers

Michael Wilkes
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It's hard to argue against "cost-effectiveness," as long as it means getting great value for price paid. Who wouldn't prefer the same product at half the price, or a superior one for just a little bit more—particularly if that extra little bit is being paid by someone else? So it's hardly surprising that almost all the physicians surveyed by Ginsburg et al, using this definition of cost-effectiveness, claimed to consider it an appropriate part of their day-to-day decision making.

Before we make too much of this, however, it's worth noting that surveys test what people say, rather than what they do—so it's possible that in actual practice, many of these respondents do not actually worry about the cost of the care they deliver. Furthermore, the fact that most of the same physicians agree that "if a medical intervention has any chance (no matter how small) of helping the patient, it is the physician's duty to offer it (regardless of cost)" suggests that their commitment to cost-effectiveness may indeed be limited.

There is an inherent contradiction in a physician supporting "cost containment" and simultaneously being unwilling to spare any expense for an individual patient. This contradiction is understandable when we consider the really hard question, which the authors didn't ask. That is, "Would you consider choosing a possibly inferior result, in an individual patient, to save substantial resources overall?" This is where the rubber meets the road and where physicians are often placed in an untenable position by the simultaneous demands of the health care system, of "society" overall (demanding that we "save money"), and of patients to whom we have a fiduciary responsibility ("spare no expense to maximize my chances").

The choices are even more complex than that. Modern American society not only wants us to spend less, but also

expects us to perform miracles, given all the resources available to us. On the other side of the equation, even though we have been taught that our commitment to our patients must trump any other concerns, 43 million Americans are still uninsured, and a great many elderly cannot afford their medicines. Perhaps if we collectively did not spend so much on intensive care at the extreme ends of life, expensive new drugs that promise the possibility of marginal benefit, or ever-more-costly technologies searching for an indication, we might be willing to pay for universal access and achieve better outcomes overall. America continues to pay far more for health care than any other nation, despite the many supposedly "cost-cutting" innovations of the past decade. At the same time, we are doing no better, and in many cases substantially worse, than others who spend considerably less, according to standardized population outcome measures such as infant mortality, teenage pregnancy, or life expectancy.

In answering a related question, almost three quarters of respondents said that only patients and their physicians should "decide if a treatment is 'worth' the cost." What, then, is the role for "society" as the third party in such matters? Individual doctors and individual patients almost never pay health care bills directly, and as long as someone else is picking up the tab, it's all too easy for them to decide, together, that no cost is too steep. But we routinely decide, as a community, that some costs are indeed too steep, even when such spending would save lives. We don't pay, for example, to erect rubber barriers along every inch of our highways because that would increase our taxes. We don't force auto makers to build safer cars because they'd turn around and charge us more. We don't even demand lower speed limits because that would slow us down. So why do we allow a multitude of individual physicians to spend unlimited amounts, for the possibility of benefit, in a multitude of individual patients?

When it comes to cost-effectiveness, physicians are placed in the middle of a conundrum, with no easy choices or answers. Studies that try to understand how physicians think about this issue are useful because physicians should and must play an important role in the many discussions that will continue to arise—as advocates for those we treat, as well for our larger community. But we must also keep in mind that these issues are not ours to decide alone or in private conversations with patients and families. And we must ask ourselves harder questions, about conflicting values and interests, rather than merely affirming that apple pie is delicious, just as cost-containment is wonderful, as long as it doesn't require us to spend a single penny less.

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Journal Digest

Are naturalistic weight-reducing efforts associated with weight gain and onset of obesity in adolescent girls?

Stice E, Cameron RP, Killen JD, et al. Naturalistic weight-reduction efforts prospectively predict growth in relative weight and onset of obesity among female adolescents. *J Consult Clin Psychol* 1999;67:967-974.

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DESIGN

Prospective cohort study with 4 years of follow-up.

SETTING

Three high schools in northern California.

PARTICIPANTS

Participants included 692 girls (mean age, 15 years; 45% white) who were grade 9 students. Girls who were pregnant were excluded.

ASSESSMENT OF RISK FACTORS

Dietary restraint, self-labeled dieting, exercise for weight loss, incidental exercise (exercise for purposes other than intentional weight control) that might affect adiposity, fasting for weight loss, use of appetite suppressants or laxatives, vomiting for weight control, binge eating, and stage of pubertal development (Tanner stage) were assessed by student self-report or structured clinical interviews. Body mass index (BMI) was measured by trained research staff.

MAIN OUTCOME MEASURES

Growth in relative weight and, after excluding initially obese girls (16% of the initial cohort), the onset of obesity.

MAIN RESULTS

Analyses were adjusted for baseline BMI and sexual maturation level. Baseline BMI was not related to subsequent growth in relative weight. Baseline incidental exercise, appetite suppressant or laxative use, vomiting for weight control, and binge eating predicted relative weight gain over the 4-year study period ($P<0.05$). Dietary restraint, self-labeled dieting, and exercise for weight control predicted onset of obesity over time. For each unit of increase on the restraint scale, there was a 192% increase in the hazard for onset of obesity (hazard ratio [HR] 2.92; confidence interval [CI] 1.74-4.89; $P<0.001$). The hazard for onset of obesity was 324% greater for self-labeled dieters than for nondieters (HR 3.24, CI 1.53-6.85, $P<0.01$), and for each unit increase on the exercise scale, there was a 25% increase in the hazard for onset of obesity over the study period (HR 1.25, CI 1.08-1.45, $P<0.01$).

CONCLUSIONS

Incidental exercise, appetite suppressant or laxative use, vomiting, and binge eating predicted relative weight gain in adolescent girls. Dietary restraint, self-labeled dieting, and exercise for weight control predicted onset of obesity.

Commentary

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Research on the development of adolescent obesity is limited. This prospective study by Stice et al is one of the few studies that examine the relationship between self-employed weight control efforts and weight change and obesity. The findings show that dieting and weight loss efforts predicted increases rather than decreases in relative weight and an increased risk of onset of obesity. The findings have credibility in the context of a rising prevalence of obesity among adult women in the United States despite a dieting prevalence of more than 50%.[1]

This study is methodologically strong, with analyses controlling for initial BMI and sexual maturity level. The participants were predominantly white, and therefore, the results may not be applicable to ethnic groups with particular vulnerability to obesity. The use of self-definition for dieting and the lack of specification of the type and duration of exercise did not allow the researchers to know if participants were actually reducing calories or exercising by standard definitions. Previous studies have shown that people may attribute activities, even those that are not related to food, as "dieting" activities.[2]

The results of this study increase our understanding of the possible effects of "generic dieting," exercise for weight control, and radical weight-loss activities on weight and onset of obesity. The notion that such reported activities may be markers for adolescents who may become obese and who may benefit from early intervention is relevant to clinicians. These findings reinforce the need for clinicians to identify adolescents at higher risk, assess the meaning of dieting and exercise for weight control, and provide tailored information and interventions to prevent weight gain. The findings of this study are relevant to nurses in the areas of pediatrics, public health, and family, school, and women's health. These clinicians are in a position to initiate obesity risk assessments and primary prevention programs for adolescents. It is important that these prevention programs be accompanied by evaluations to assess their effectiveness.

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Journal Digest

In children receiving antibiotics, does coadministration of *Lactobacillus* GG reduce the incidence of diarrhea?

Vanderhoof JA, Whitney DB, Antonson DL, et al. Lactobacillus GG in the prevention of antibiotic-associated diarrhea in children. *J Pediatr* 1999;135:564-568.

DESIGN

Randomized, placebo-controlled trial with 10 days of follow-up.

PATIENTS

A total of 202 children in Rapid City, SD between 6 months and 10 years of age who had an acute infection of the upper or lower respiratory tract, urinary tract, soft tissues, or skin and for whom a 10-day course of antibiotics was prescribed. Exclusion criteria were chronic disease, serious acute infection, or diarrhea at the start of antibiotic administration. A total of 188 children (93%) (median age, 4 years; 55% girls) completed the study.

INTERVENTION

Children were allocated to receive *Lactobacillus* GG (CAG Functional Foods, Omaha, NE) (n=93) or placebo (n=95). Children who weighed less than 26 lb (<12 kg) took 1 capsule (10^{10} colony-forming units of live *Lactobacillus* GG) daily with meals, and those who weighed 26 lb or more (≥12 kg) took 2 capsules (2×10^{10} colony-forming units).

MAIN OUTCOME MEASURES

Incidence of diarrhea (≥2 liquid stools per day on ≥2 occasions), stool frequency, and stool consistency (rated on an 8-point scale: 1=watery, 4=loose and soft, and 8=hard and dry).

RESULTS AND CONCLUSIONS

Fewer children who received *Lactobacillus* GG had diarrhea than did those who received placebo ($P<0.001$) (table). The mean duration of diarrhea was slightly shorter in the group receiving *Lactobacillus* GG than in the placebo group (4.7 vs 5.9 days, $P = 0.05$). By day 10, stool frequency was lower in the *Lactobacillus* GG group than in the placebo group (mean number of stools per day, 1.4 vs 2.0; $P<0.02$). By day 7, fewer children who received *Lactobacillus* GG had a stool consistency score of less than 4 than did patients who received placebo ($P<0.001$) (table). Coadministration of *Lactobacillus* GG can reduce the incidence and duration of diarrhea, stool frequency, and watery or soft stool consistency in children treated with antibiotics.

Lactobacillus GG (LGG) *versus placebo for diarrhea in children receiving antibiotic therapy for 10 days**

Outcomes	LGG	Placebo	RRR (95% CI)	NNT (CI)
Diarrhea	8	26	71 (39-87)	6 (4-13)
Stool consistency <4†	17	48	64 (43-78)	4 (3-6)

RRR = relative risk reduction, NNT = number needed to treat, and CI = confidence interval.
*Data are percentages and have been calculated from data in the article.
†Stool consistency score <4 means that stool consistency ranged from loose and soft to watery.

Commentary

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Gastrointestinal upsets are a well-known side effect of broad-spectrum antibiotic therapy. Although generally regarded as normal, diarrhea arising from the disturbance of the gastrointestinal microflora is often enough to cause parents to discontinue the antibiotics prescribed for their children.

In recent times, the consumption of live microbial organisms, or probiotics, as they are collectively known, has been advocated both for improving health and preventing disease. With the discovery of organisms able to withstand the action of gastric secretions and bile, claims of the ability of probiotics to maintain the microbial balance of the intestine during antibiotic therapy have gained momentum.

The trial by Vanderhoof et al examined the influence of probiotic organism ingestion on gastrointestinal side effects during antibiotic therapy, and their results support the use of probiotics. The findings indicate that 6 children would need to be given *Lactobacillus* GG to prevent 1 additional child from having antibiotic-induced diarrhea, and 4 children would need to be given *Lactobacillus* GG to prevent 1 additional child from having loose and soft or watery stools by day 7 of treatment.

The strength of the study lies in the blinding of all parents, clinicians, and researchers to the intervention. In part, this compensates for the fact that the outcome measures studied were subjective assessments made by parents. In addition to validating parental reports of children's gastrointestinal symptoms, information about the child's usual bowel habits and results of stool cultures[1] would have strengthened the design. Also, the study was funded by the company that produces the drug, a fact that should alert the reader to possible bias.

Despite these design weaknesses, the results confirm the findings of an earlier study[1] and indicate that the use of *Lactobacillus* GG may reduce gastrointestinal upsets associated with antibiotic therapy. Nurses and clinicians seeking to minimize antibiotic-induced diarrhea should consider the use of probiotics. Further research is needed about the effect of reducing antibiotic-induced diarrhea on child absenteeism from school and day care, the use of health services, and compliance with antibiotic treatment.

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Medicine Cabinet

Drug treatment of multiple sclerosis

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Competing interests: Both authors have received research grants and lecturing and consultancy fees from various pharmaceutical companies dealing with multiple sclerosis, including those that manufacture the various forms of interferon beta and glatiramer acetate.

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Multiple sclerosis is the most common cause of chronic neurologic disability in young adults, with a prevalence of about 1 in 1,000. About 50% of patients are unable to walk without assistance 15 years after onset. As yet, no treatment can halt the accumulation of disability. In recent years, however, there has been substantial progress in understanding the pathogenetic mechanisms of the disease and in developing techniques to monitor treatment. Based on this progress, treatments were developed that have a favorable effect on the natural course of the disease (disease-modifying drugs). We discuss the evidence available from large randomized, placebo-controlled studies, and we address several questions that still generate wide interest in relation to treatment with disease-modifying drugs. The treatment of symptoms and rehabilitation, which still remain the mainstay of care of most patients with multiple sclerosis, are not reviewed here.

Summary points

- Disease-modifying treatment should be considered early in the course of multiple sclerosis for patients with an unfavorable prognosis
- Considerable dispute exists among experts about the optimal time to start treatment
- Interferon beta is the first-line treatment of relapsing-remitting multiple sclerosis
- Glatiramer acetate—although not yet available in several European countries—has comparable efficacy in relapsing-remitting multiple sclerosis
- Future trial results are crucial to assess the role of interferon beta in secondary progressive multiple sclerosis
- Magnetic resonance imaging has an important role in better understanding the treatment response in multiple sclerosis

METHODS

We have concentrated mainly on drugs that have been specifically approved for use in multiple sclerosis. Our sources included articles from MEDLINE, information from international meetings on multiple sclerosis, and ongoing discussions with colleagues.

MULTIPLE SCLEROSIS

Clinical course

Multiple sclerosis usually manifests clinically in the third or fourth decade, typically presenting with a relapsing-remitting course that, after an average of 5 to 15 years in most patients, is followed by the onset of the so-called secondary progressive phase. Secondary progression can occur in the presence or absence of superimposed relapses. A subgroup of patients labeled with relapsing-remitting disease show a relatively benign course with little or no disability after 10 or more years. About 10% of patients have a primary progressive course from the onset, without clinical relapses. Rarely, patients have malignant multiple sclerosis with a rapidly progressive course. The ability to predict the development of disability in a disease as variable as multiple sclerosis is a major challenge. Although unfavorable prognostic features have been recognized (box), their power to give an accurate prognosis for individual patients is modest at best.[1]

Factors associated with unfavorable prognosis in multiple sclerosis

- Male sex
- Older age at onset
- Motor or cerebellar signs at onset
- Short interval between initial and second attack
- High relapse rate in early years
- Incomplete remission after first relapses
- Early disability
- High lesion load detected by early magnetic resonance imaging of the brain

Cause

Epidemiologic evidence has long suggested that 2 factors are involved in causing multiple sclerosis: exposure to an environmental agent and genetically determined susceptibility. The environmental agent is widely assumed to be infective, most likely viral, but all evidence is indirect and inconclusive, and only few think that there is a single unique virus that causes multiple sclerosis. Genetic studies have convincingly shown that there is not 1 single unique gene for multiple sclerosis: multiple genes are involved,[2] but how the genetic factors operate and how they interact with the environmental agents in establishing the disease is largely unknown.

Pathogenesis

The widespread belief, although unproved, is that multiple sclerosis is an organ-specific autoimmune disease orchestrated by autoreactive T cells. Activation of these autoreactive T lymphocytes in the systemic circulation may enhance their movement through the blood-brain barrier, which then leads to multifocal sites of perivascular cuffing of lymphocytes and destruction of myelin sheath within

the central nervous system. To date, however, evidence of a unique immunologic abnormality in patients with multiple sclerosis is lacking. In particular, T cells that recognize myelin can be identified with similar frequency in patients with and without multiple sclerosis.

Studies on the disease have suggested a noticeable heterogeneity in disease pathogenesis[3]; at least 4 different histologic patterns of the lesion were shown. For example, in some cases, the process seems to be directed primarily at the myelin sheath, with relative sparing of oligodendrocytes, whereas in other cases, there is primary destruction of oligodendrocytes. Although the lesion of multiple sclerosis is primarily inflammatory and demyelinating, recent evidence reemphasizes that axonal loss may occur early in the disease course and that it is critically important in the development of irreversible disability.

MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) has both improved the diagnostic accuracy of multiple sclerosis and played an important role in better understanding the natural history of the disease. Patients with frequent relapses often exhibit new lesions after enhancement with gadolinium, indicating focal breakdown of the blood-brain barrier. Secondary or primary progression is associated with markers of tissue destruction, as shown by MRI (increased volume of T1 hypointense lesions, reduced magnetization transfer ratio, progressive atrophy), rather than new activity of focal lesions.

In addition, magnetic resonance imaging has prognostic and therapeutic applications: the amount of lesions in the early phases of the disease predicts future disability, and quantification of disease activity (lesions shown after enhancement with gadolinium, new lesions) and lesion burden provides a powerful tool in therapeutic trials.[4,5]

CLINICAL TRIALS

Advances in the treatment of multiple sclerosis depend on clinical trials because of the highly variable and unpredictable course of the disease and the difficulty in precisely measuring neurologic disability. Because progression of the disease in general is slow, these clinical trials traditionally require a relatively large number of patients and long follow-up.

The past decade has seen an increasing ability to perform preliminary examination of the effect of new treatments by using MRI as an outcome measure. The advantage of MRI is its high reproducibility and its high sensitivity in detecting disease activity, which is 5- to 10-fold more frequent than clinical relapse.[5]

TREATMENT

The possibilities for the treatment of multiple sclerosis depend on the clinical situation. We address separately treatment of relapse and disease-modifying treatment in patients with relapsing-remitting disease and those with the secondary progressive phase of the disease.

Treatment of relapse

The treatment of relapse is irrespective of whether it occurs in patients with relapsing-remitting disease or those with the secondary progressive phase of the disease. Although almost all patients with relapse show some degree of spontaneous recovery, most clinicians advise treatment of relapse that has an important effect on function. For many years, corticosteroids have been the first-choice treatment. Corticosteroids shorten the duration of the relapse and accelerate recovery, but there is no convincing evidence that the overall degree of recovery or the long-term course of the disease is affected.

The most commonly applied regimen consists of a brief course of high-dose methylprednisolone sodium succinate given intravenously IV (500-1,000 mg per day for 3-5 days). Some clinicians substitute oral prednisone for IV methylprednisolone because it is easier to use and costs less. Data substantiating the comparable benefits of oral prednisone and IV methyprednisolone in acute relapses have been presented but are not definitive.[6] In various studies—all of them small—different dosage regimens of oral steroids have been applied.[7]

Disease-modifying treatment of relapsing-remitting multiple sclerosis

The goal of treatment in patients with relapsing-remitting multiple sclerosis is to reduce the frequency and severity of relapses (and thereby prevent exacerbations) and to prevent or postpone the onset of the progressive phase of the disease. To achieve this goal, in the past especially, immunosuppressive drugs were used, but they have never found widespread acceptance owing to limited efficacy and considerable toxicity.

More recently, large randomized controlled trials have been performed successfully with interferon beta-1a, interferon beta-1b, and glatiramer acetate.[8-11] These substances should be seen as immune modulators rather than immune suppressors. The trials have led to the regulatory approval of 4 agents—Avonex, Biogen, United States; Betaseron, Berlex, United States (Betaferon, Schering, Germany); Copaxone, Teva, Israel; and Rebif, Serono, Switzerland—for reducing the severity and frequency of relapses (table).

Interferon beta

Currently 2 forms of recombinant interferon beta, interferon beta-1a and interferon beta-1b, have been approved by US and European regulatory authorities for the treatment of relapsing-remitting multiple sclerosis. Interferon beta-1a (Avonex, Rebif) is a glycosylated, recombinant product from mammalian cells, with an amino acid se-

Clinical results of lagre randomized trials

Trial	Agent	Drug name	Disease type	Primary outcome	Result on primary outcome
Jacobs et al, 1998[8,16]	Interferon beta-1a	Avonex	Relapsing-remitting	Time to confirmed progression	Positive
	Interferon beta-1a	Avonex	Secondary progressive	Time to confirmed progression	Trial still ongoing
	Interferon beta-1a	Avonex	After 1st attack	Time to 2nd attack	Positive
	Interferon beta-1a	Avonex	Primary progressive	Time to confirmed progression	Presented as negative; not yet published
PRISMS Study Group, 1998[9]	Interferon beta-1a	Rebif	Relapsing-remitting	Relapse rate	Positive
SPECTRIMS study*	Interferon beta-1a	Rebif	Secondary progressive	Time to confirmed progression	Presented as negative
Comi et al, 1995[15]	Interferon beta-1a	Rebif	After 1st attack	Time to 2nd attack	Presented as positive; not yet published
INFB Multiple Sclerosis Study Group, 1993	Interferon beta-1b	Betaseron	Relapsing-remitting	Relapse rate	Positive
European Study Group, 1998[20]	Interferon beta-1b	Betaseron	Secondary progressive	Time to confirmed progression	Positive
	Interferon beta-1b	Betaseron	Secondary progressive	Time to confirmed progression	Presented as negative; not yet published
Johnson et al, 1995[11]	Glatiramer acetate	Copaxone	Relapsing-remitting	Relapse rate	Positive

*Abstract only; not yet published.

quence identical to that of natural interferon beta. Interferon beta-1b (Betaseron [Betaferon]) is a nonglycosylated recombinant product from bacterial cells in which serine is substituted for cysteine at position 17.

All 3 drugs have been studied in large double-blind placebo-controlled randomized clinical trials.[8-10] Inclusion in these studies was restricted to patients with clinically active disease in the years before entry to the study (2 exacerbations in 2 years for Betaseron and Rebif; 2 in 2 years for Avonex) who had mild to moderate disability and essentially were fully ambulatory (expanded disability status scale, 0-5.5 for Betaseron; 0-5 for Rebif; and 1-3.5 for Avonex). The most prominent clinical result of all trials was a clear reduction in both frequency (by about a third) and severity of exacerbations. These observations with regard to treatment effect were supported by convincing findings on MRI both as a reduction of active lesions and as a positive effect on total lesion load in the brain.[12-14] Because of the robustness of the evidence, most experts consider interferon beta as first-choice treatment in patients with relapsing-remitting multiple sclerosis. Many issues related to treatment with interferon beta, however, remain unresolved (box).

Unresolved issues in treatment with interferon beta

- Optimal moment of initiation of treatment
- Optimal dose, frequency, and route of administration
- Long-term effects of treatment
- When to stop treatment
- Occurrence and relevance of neutralizing antibodies
- Mechanism of action
- Cost utility

When to start and stop interferon beta

In individual patients, decisions on the initiation of treatment should be based on the course of the disease, but about 10% to 20% of patients have relatively benign disease, so they may not require disease-modifying treatment. Treatment should not be postponed until after persistent neurologic deficits have occurred because interferon beta does not reverse fixed deficits. Disease-modifying treatment should be considered early in the course of disease for patients with an unfavorable prognosis, but the rate and pattern of progression of disease cannot be reliably predicted at initial assessment. Whether long-term treatment should start at the time of the first attack, which seems to be sensible for preventive therapy, was addressed in 2 placebo-controlled studies.[15,16] These studies showed that low-dose interferon beta-1a reduces the likelihood of a second episode in the 2 or 3 years following a first episode suggestive of multiple sclerosis in patients who have prognostically unfavorable findings on MRI.

Most guidelines concerning treatment with interferon beta in relapsing-remitting multiple sclerosis are based on the inclusion criteria that have been used in the placebo-controlled trials mentioned above. Patients with definite relapsing-remitting disease who have had at least 2 relapses in the past 2 or 3 years and who are still able to walk without support for at least 100 m are considered eligible for treatment. It is extremely important that before these long-term treatments are implemented, counseling about

realistic objectives, both regarding efficacy and side effects, takes place because overly optimistic expectations may complicate treatment.

Whether treatment should be discontinued at some time is currently unknown because limited information is available on the long-term effects of interferon beta. Current guidelines on stopping treatment are related to side effects, desire to become pregnant, and perceived inefficacy as shown by frequent relapses or progression of disability during treatment.

Choice of drug

Direct comparisons have not been made between the different interferon beta preparations, and therefore, definite conclusions from the published data about the superiority of 1 preparation over the other are not possible. The main differences between the registered drugs are the amount of interferon beta given and the route and frequency of administration: Avonex, 6 million units (30 µg) by intramuscular injection once a week; Betaseron, 8 million units (250 µg) by subcutaneous administration every other day; and Rebif, 6 million units (22 µg) by subcutaneous administration 3 times a week. Treatment with any of these drugs is usually well tolerated.

One study compared 3 dosages of interferon beta-1a given subcutaneously once a week with placebo and showed increasing treatment effect with increasing dosage, thereby suggesting that some of the currently applied dose regimens might be suboptimal.[17]

Cost utility

Quality of life has been shown to be substantially reduced in patients with multiple sclerosis, and it would be important to know whether interferon beta has a favorable effect on quality of life. Although it is likely that a reduction in frequency and severity of attacks makes a difference to the quality of life of a patient with multiple sclerosis, studies have so far not provided firm evidence for this. Models based on assumptions (on costs and savings) and estimates of long-term gains have been described, concluding that treatment with interferon beta has a high cost per quality-adjusted life-years gained.[18]

Glatiramer acetate

Glatiramer acetate (Copaxone) is a synthetic copolymer with some immunologic similarities to myelin basic protein, 1 of the major components of myelin. Daily treatment with subcutaneous administration of 20 mg of glatiramer acetate resulted in a 29% reduction of the annual relapse rate in a 2-year trial.[11] These clinical observations were later supported by findings on MRI in a separate study.[19] Adverse effects of glatiramer acetate are usually mild. Definitive data on the effect of glatiramer acetate on disease progression are not available.

Glatiramer acetate was approved by the US authorities in 1996, but so far there is no pan-European license. The indications for the use of glatiramer acetate are comparable to those for interferon beta, but most clinicians consider it as second-line treatment of relapsing-remitting multiple sclerosis.

Disease-modifying treatment of secondary progressive multiple sclerosis

The goal of treatment in patients with secondary progressive multiple sclerosis is to prevent progressive worsening of the disease. Until recently, no agent had a favorable effect on the disease once it had entered the secondary progressive phase.

Interferon beta

A randomized, double-blind, placebo-controlled, multicenter trial of interferon beta-1b (8 million units subcutaneously every other day) was recently completed in Europe, including 718 patients with clinically active secondary progressive multiple sclerosis.[20] At the predetermined interim analysis, the study was stopped because of a significant difference in the time to confirmed neurologic deterioration in favor of the treated group. The delay of progression was about 9 to 12 months. Significant reductions were also observed in time to become wheelchair bound, number of steroid courses given, and number of admissions to a hospital because of multiple sclerosis. Based on these results, interferon beta-1b was approved for use in patients with secondary progressive multiple sclerosis in Europe.

Recently it was reported that in a large placebo-controlled trial, interferon beta-1a (Rebif) failed to have a major effect on disease progression (the Secondary Progressive Efficacy Clinical Trial of Recombinant Interferon Beta-1a in Multiple Sclerosis [SPECTRIMS] study, 9th meeting of the European Neurological Society, Milan, 1999). So far, these results have been published only in abstract form. Full publication of the results is eagerly awaited, as are the detailed results of a second study of interferon beta-1b in patients with secondary progressive multiple sclerosis that was carried out in the United States.

The question of when to start and stop interferon beta in secondary progressive disease is difficult to answer; evidence should be reviewed as the detailed results of further trials become available (table). It is likely that these results will also have an effect on the outcome of cost-utility studies in secondary progressive multiple sclerosis.[21]

Role of traditional immunosuppressants

Given that both interferon beta and glatiramer acetate, although convincingly shown to be effective, have major limitations, including cost, inconvenience (given parenterally), and a relatively modest overall effect on disease course, several experts have urged reconsideration of the role of immunosuppressants like azathioprine or metho-

trexate. Compared with interferon and glatiramer acetate, these drugs are much cheaper, easier to give, and might also have a favorable effect on the natural course of the disease.[22,23] The lack of convincing data for immunosuppressants from MRI—as opposed to interferon beta and glatiramer acetate—has probably contributed to their rather modest acceptance. This is especially important now that MRI has achieved more widespread acceptance as a surrogate marker of disease progression owing to better understanding of its correlation with both clinical disability and underlying pathology of disease.

NEW DEVELOPMENTS

A whole range of new treatment strategies is under investigation, varying from subtle immune interventions, such as the induction of immune tolerance or administration of various monoclonal antibodies, to aggressive strategies such as bone marrow transplantation.[24] Recent observations of axonal damage early in the disease course and increasing disability despite optimal anti-inflammatory treatment emphasize the need for rigorous investigation of neuroprotective treatment.[25-27]

Many experts think that various treatment strategies should be combined to be optimally effective. Alternatively, if preliminary neuropathologic observations indicating that individual patients may have unique mechanisms underlying their disease process would be confirmed, it could be possible in the future to tailor treatment on the basis of individual patient characteristics.[28]

CONCLUSIONS

The introduction of interferon beta and glatiramer acetate as drugs effective in modifying the course of relapsing-remitting multiple sclerosis has improved the treatment of multiple sclerosis and provided tools to unravel further the mechanisms of the disease.

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Best Practice

TOPICS IN REVIEW

Chest pain evaluation units

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Chest pain is a common cause of emergency department (ED) presentation. In the United States, it accounts for 5% to 6% of new ED attendances.[1,2] The principal challenge in these patients is to identify those with an acute coronary syndrome. Early diagnosis allows effective treatment, and premature discharge may have disastrous consequences for patient and doctor: in the United States, between 2% and 5% of patients with acute myocardial infarctions are discharged from the ED, and 20% of malpractice claims against emergency physicians relate to the management of acute coronary syndrome.[3]

The problem with the emergency assessment of these patients lies in the limitations of diagnostic tests for acute coronary ischemia—electrocardiography (ECG) is diagnostic of acute myocardial infarction in only 40% to 65% of patients and is even less useful in those with unstable angina.[4] Despite recent advances, serum markers for myocardial necrosis detect, at best, 66% of patients with acute myocardial infarction on arrival.[5] Faced with these diagnostic difficulties and the consequences of misdiagnosis, ED physicians have a low threshold for admitting patients with chest pain in whom the diagnosis is not immediately clear. Some 60% to 65% of these patients have an eventual diagnosis of noncardiac chest pain,[3] and although serious disease is diagnosed in a few, this traditional approach to chest pain is both time-consuming and expensive.

It is against this background that the concept of ED-based chest pain evaluation units emerged, with the aim to provide medically equivalent care at a lower cost for patients presenting to an ED with chest pain with a probability for acute coronary syndrome that is low, but not sufficiently low to allow discharge. The concept originated in, and has been almost exclusively confined to, the United States. The first chest pain evaluation unit was set up in 1981 and, by 1997, 15% of EDs in the United States had followed suit.[6] In this article, I review the literature on chest pain evaluation units to answer the following questions:

- How are patients managed on chest pain evaluation units?
- Is there evidence for their clinical effectiveness?
- Are they cost-effective?
- Is there evidence of patient satisfaction?

SEARCH METHODS

A literature search was carried out to identify research articles and those whose principal focus was chest pain evaluation units run by EDs for the assessment of chest pain of possible cardiac origin. The following databases were searched: MEDLINE, EMBASE, the Cochrane Library, and the Database of Abstracts of Reviews for Effectiveness. The following search terms were used: "emergency service, hospital," "myocardial infarction/diagnosis," "myocardial ischemia/diagnosis," "angina pectoris/diagnosis," "chest pain/diagnosis," "chest pain/therapy," "cost-benefit analysis," and "randomized controlled trials." In addition, the reference lists of retrieved articles were searched for those not identified in the computerized search. Journals were not hand-searched, and authors were not contacted for unpublished work. Articles were selected if they described patient management or presented evidence for clinical efficacy, cost-effectiveness, or patient satisfaction. Where appropriate, articles were critically appraised along standard guidelines.[7,8] Conference abstracts were not selected because the brevity of information hinders meaningful critical appraisal.

RESULTS

Patient management

Eight articles were identified that described the management process in 6 chest pain evaluation units. These are summarized in table 1.[9-14] Despite differences in the detail, the overall approach to patient management is similar in the different centers. All are described as being located in, or adjacent to, the ED. All centers include patients with nontraumatic chest pain deemed to be at low risk for acute myocardial infarction. In 4 centers, the ascription of risk is at the discretion of the treating physician, according to local guidelines. In the other 2 units, risk is determined according to the Goldman algorithm, a validated tool that divides patients with chest pain into groups with differing probabilities of acute myocardial infarction, based on history, examination, and ECG findings.[15] Patients are eligible for these chest pain evaluation units if they have a probability of acute myocardial infarction that is calculated to be less than 7%.

Exclusion criteria are described for 5 of the centers. Common exclusion criteria are ECG evidence of acute myocardial ischemia or the presence of complications of cardiac ischemia (for example, arrhythmia, hypotension, congestive cardiac failure, and prehospital cardiac arrest). The identification of a noncardiac diagnosis is stated as an exclusion criterion in 4 of the 5 centers. Two units exclude patients with a history of coronary artery disease, and 1 specifically includes these patients. The inability to perform an exercise test excludes patients in 1 center.

Table 1 *Management protocols in 6 chest pain evaluation units*

Study, year	Duration of protocol, hr	ECG	Biochemical markers	Additional testing
Zalenski et al,[9] 1997	12	0, 6, and 12 hr	CK-MB at 0, 4, 8, and 12 hr	Exercise tolerance testing (ETT)
Gibler et al,[10] 1995	9	Continuous ST segment monitor	CK-MB at 0, 3, 6, and 9 hr	2-dimensional echo, ETT
Hoekstra et al,[11] 1994	9	Continuous ST segment monitor	CK-MB at 0, 3, 6, and 9 hr	Thallium ETT
Doherty et al,[12] 1994	9	0, 3, 6, and 9 hr	CK-MB at 0, 3, 6, and 9 hr	Cardiology consultation, ETT, thallium ETT, MUGA scan
Mikhail et al,[13] 1997	8	Continuous ST segment monitor	Total CK at 0 hours; with or without CK-MB at 0, 4, and 8 hr; with or without myoglobin at 0 and 4 hr	ETT, stress echo, dobutamine echo, thallium ETT
Gomez et al,[14] 1996	9	Continuous ST segment monitor	Total CK and CK-MB at 0, 3, 6, and 9 hr	ETT, dobutamine echo

ECG = electrocardiography; CK-MB = creatine kinase–muscle-brain isoenzymes; echo = echocardiography; MUGA = multigated angiocardiography.

Once admitted to the units, patients receive serial clinical, ECG, and biochemical assessment at specified intervals. If evidence of acute myocardial infarction or unstable angina emerges, the patient is transferred to a critical care unit. Patients with normal results at the end of the testing period undergo exercise stress testing or an equivalent in those physically unfit for the treadmill. If these tests are positive, the patient is admitted for further evaluation. If negative, the patient is discharged home. Follow-up is arranged with a cardiologist or family physician.

Clinical efficacy

An effective chest pain evaluation unit should have a diagnostic protocol that performs as well as standard management. The gold standard for evaluating a new diagnostic test (chest pain evaluation unit) entails its independent, blind comparison with a reference standard of diagnosis (standard inpatient management), the reference being applied irrespective of the new test result.[16] Five published studies have assessed the diagnostic utility of their chest pain evaluation unit's protocol, but only 1 meets the above criterion. Zalenski et al[9] studied 317 patients, all of whom were initially admitted to a chest pain evaluation unit. At the end of the testing protocol, all patients were admitted to the hospital for the establishment of reference diagnoses according to the standard inpatient examination. Final reference diagnoses were assigned by a physician blinded to the results of the chest pain evaluation unit outcomes. The sensitivity and specificity of the protocol for acute coronary insufficiency were 90.0% (95% confidence interval [CI], 73.4%-97.9%) and 50.5% (95% CI, 44.6%-56.4%), respectively. Negative and positive predictive values were 98.0% (95% CI, 94.2%-99.6%) and 16.0%, respectively. The authors assume a sensitivity of 100% for the inpatient protocol.

Four other articles used the incidence of adverse outcomes over a period of follow-up as a measure of the diagnostic accuracy of their protocol. Table 2[10,12-14] summarizes the results.

The proportion of patients discharged home after the protocol, the duration of stay, and the frequency with which ischemic heart disease is diagnosed in all chest pain unit patients and in those admitted with positive results all relate to the effectiveness of the unit. Table 3[10,12-14,17] summarizes the available evidence on these issues.

Table 2 *Outcomes of patients discharged from 4 chest pain evaluation units*

Study, year	No. of patients*	Period of follow-up	Adverse outcomes
Doherty et al,[12] 1994	176	9 mo	None
Mikhail et al,[13] 1997	410	5 mo	1 acute MI at 6 days
Gibler et al,[10] 1995	829	1 mo	1 acute MI at 3 days; 4 noncardiac deaths at 1 mo
Gomez et al,[14] 1996	46	30 days	None

MI = myocardial infarction.
*Number of patients discharged after negative evaluation in chest pain unit.

Cost comparisons

Four articles report comparative studies, with cost as a primary outcome. Roberts et al[18] randomly allocated 166 patients eligible for the chest pain evaluation unit to either the chest pain unit (intervention) or standard inpatient treatment (control). The mean total cost per chest pain

Table 3 *Outcomes of patients admitted to chest pain evaluation units (CPEUs)*

Study, year	No. of patients	Discharged, no. (%)	Duration (control), hr	% Admitted with ACS*	% CPEU patients with ACS†
Gomez et al,[14] 1996‡	50	46 (92)	15.4 (54.6)	25	2
Doherty et al,[12] 1994	226	176 (78)	17.4 (52.87)	10	2
Toner,[17] 1997	1,724	1,233 (72)	6.5	NS	NS
Gibler et al,[10] 1995	1,010	829 (82)	NS	28	4
Mikhail et al,[13] 1997	477	410 (86)	NS	66	9

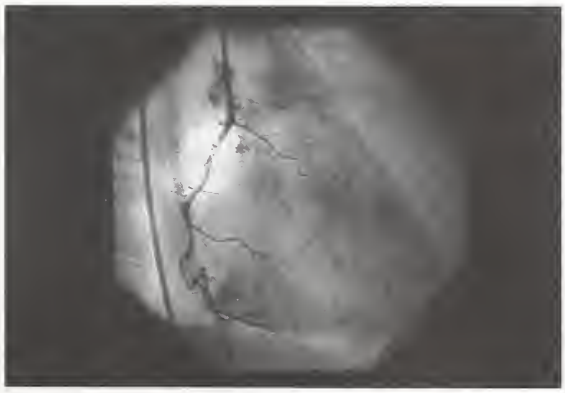
ACS = acute coronary syndrome; NS = not stated.
*Percentage of patients admitted from the CPEU with an eventual diagnosis of an acute coronary syndrome.
†Percentage of all patients admitted to the CPEU with a final diagnosis of an acute coronary syndrome.
‡This study was a randomized controlled trial.

unit patient was $1,528 compared with $2,095 for controls ($P$<0.01). Mean costs for patients admitted after chest pain unit evaluation were $2,410, higher than the cost for patients discharged after chest pain unit evaluation ($803, P<0.001) and for controls ($2,095, P<0.13). This study was well designed with robust randomization, clearly stated sample size calculations, intention-to-treat analysis, and rigorous cost analysis. Blinding was not possible because patients were managed in different areas.

In a second randomized controlled trial, Gomez et al[14] reported mean hospital charges of $1,297 in the chest pain unit group versus $5,719 in the routine care (control) group (P<0.001). Figures are not presented for the cost differences between those admitted from the chest pain unit and those discharged.

Mikhail et al[13] report a comparative study using retrospective controls. The mean total cost per case for patients discharged from the chest pain unit was $894. The corresponding figure for controls was $2,364.

In another nonrandomized trial, Hoekstra et al[11] report a cost analysis for chest pain units in 2 centers. Patients admitted to the hospital when the chest pain units were full were used as controls. In both centers, mean charges were significantly less for chest pain unit patients than for controls (center 1: $2,797 vs $3,957 [$P$<0.01]; center 2: $1,931 vs $3,961 [$P$<0.01]). This article also reports higher mean charges in patients admitted following chest pain unit evaluation than in controls, although these differences were not statistically significant.



Mehau Kulyk/SPL

Dedicated chest pain units aim to detect patients with coronary artery disease, as is the reason for this angiogram

Patient satisfaction

Rydman at al[19] report a randomized controlled trial comparing patient satisfaction between those admitted to a chest pain observation unit and controls admitted for routine care, using patient interviews to score a number of satisfaction markers from 1 (most dissatisfied) to 4 (most satisfied). The chest pain unit scored higher than inpatient management on all 7 satisfaction indices, with the attainment of a statistically significant difference in 4 of these scores.

DISCUSSION

The management strategy used in chest pain evaluation units represents a condensed form of traditional inpatient management. Protocols differ in some of their components, although no study has compared 1 with another. Recent evidence on the performance of troponin T and troponin I assays in patients with chest pain and normal ECGs offers the prospect of even shorter testing periods. In a well-designed validation study, Hamm et al[5] report that troponin T and troponin I tests were positive in 94% and 100% (respectively) of patients with acute MI within 6 hours of pain onset, although this study was not carried out in the context of a chest pain unit.

All units perform some form of provocative testing before discharge. This practice recognizes the safety of early exercise testing in patients with chest pain who have a low risk of acute coronary syndrome[20,21] and the dangers of omitting such testing—Gaspoz et al[22] reported a 1.2% missed MI rate in patients discharged from a cardi-

ology-run chest pain observation unit, only 19% of whom had had an exercise test before discharge.

It is clear that the success of these units stands or falls on rapid and extended access to cardiac enzyme assays and stress testing facilities. Most of the reporting US centers can access blood assays 24 hours a day and exercise testing 7 days a week. Excluding patients unable to perform exercise tests may simplify the logistics by obviating the need for rapid access to more sophisticated provocation tests but would probably limit the usefulness of the unit.

Despite the considerable investment required, chest pain units may have a modest effect on chest pain management in a given department. In a feasibility study, Zalenski et al[1] found that only 28% of patients deemed to be at low risk for myocardial infarction were eligible for the chest pain unit. Characteristics of the study population, protocols used, and chest pain unit exclusion criteria all affect this proportion.

The available evidence suggests that chest pain evaluation units deliver what they promise, providing equivalent clinical outcomes to inpatient management, in a shorter time and for lower cost. Follow-up of discharged patients has demonstrated the safety of the protocols, although given the sensitivity of 90% reported by Zalenski et al,[9] and with a disease prevalence of 10%, about 1 of 100 tested patients would be wrongly classified as disease free. The specificities of the protocols are moderate, and most patients admitted to the hospital after having had positive findings in the chest pain unit prove ultimately not to have an acute coronary syndrome (table 3). This underscores the limitations of current diagnostic tests.

Two well-designed studies have demonstrated the cost benefits of chest pain evaluation units. The important observation is that patients managed on the unit who are subsequently admitted to a hospital cost more than those managed in the routine way. Savings can be made only if most of those managed on the unit are discharged. Most units achieve this (table 3). It is probable that some patients will be admitted to the unit who would otherwise have been discharged after initial evaluation. This is essential to decrease missed MI rates but will affect overall cost-effectiveness.

There is a potential in chest pain evaluation units to overlook other causes of chest pain, given the overwhelming focus on excluding cardiac disease. Many of these alternative diagnoses are not readily apparent, and some may have serious consequences. In addition, chest pain evaluation units run the risk of downplaying the importance of symptoms other than chest pain in the presentation of myocardial ischemia. These possible pitfalls have received little attention in the literature, although it seems likely that focused education would lessen the risk.

It is estimated that, since 1991, more than 500 chest pain evaluation units have been established in EDs across the United States.[23] There are no published reports of such emergency department-based units from any other country. Retrospective denial of payment for patients admitted with noncardiac chest pain is not an uncommon occurrence in the United States,[3] and it is clear from the literature that financial pressures have had an important role in the development of chest pain evaluation units. Of the 3 randomized controlled trials identified, 2 focus on cost. The clinical benefits are largely reported in observational studies. Whatever their origin, the role of chest pain units continues to develop in the United States, with the recent publication of the results of a randomized trial reporting the safe, clinically and cost-effective use of a chest pain observation unit for the treatment of patients with unstable angina deemed to be at intermediate risk for cardiac events.[24]

CONCLUSION

Experience in the United States has demonstrated that chest pain units manage patients at low risk for myocardial infarction as effectively as inpatient admission and at less cost. They seem like a good idea. However, all available evidence emanates from the United States and may not be generalizable to other countries.

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Withdrawal of medical treatment in children

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Summary points

- There are 5 circumstances in which withdrawal of support may be considered in children—brain death, permanent vegetative state, "no chance", "no purpose," and "unbearable"
- Effective palliative care must be provided after withdrawal of curative treatment
- Good communication between the medical staff and parents minimizes dissent between the 2 parties
- Children with disabilities can have a quality of life that is acceptable to them and their parents, and they should not be discriminated against
- The family needs support after the death of a child

INTRODUCTION

Children are not supposed to die. In developed countries, the majority of pediatric deaths occur in a hospital, usually in an intensive care setting. Studies performed in various centers over the past decade have shown that withdrawal or withholding of support accounts for between 28% and 65% of deaths in pediatric intensive care units (see table).[1-6]

The United Kingdom's Royal College of Paediatrics and Child Health recently published a practice framework to address the circumstances in which intensive treatment may not be in the best interest of a child.[7] This article reviews each of the 5 scenarios envisioned by the college and provides illustrative case histories. To protect patient confidentiality, all of these cases are composites. I also outline the importance of good communication between medical staff and the family, together with options when dissent arises between the 2 parties.

CIRCUMSTANCES IN WHICH WITHDRAWAL OF TREATMENT MAY BE CONSIDERED

The brain dead child

When brain death is confirmed—after all potentially reversible causes have been excluded—a child is, by definition, dead. The diagnosis must be confirmed by another physician. Each state in the United States has its own laws regarding the determination of brain death. The majority use the Uniform Determination of Brain Death Act. This describes death as having taken place when someone has had irreversible cessation of all functions of the brain, including the brain stem. No confirmatory laboratory tests are required, but a second physician must independently confirm the diagnosis of brain death, and neither of

Mode of death (%) in pediatric intensive care units

	Washington DC[1]	Salt Lake City, UT[2]	Chicago, IL[3]	Alberta, Canada[4]	Lille, France[5]	London, England[6]
Withdrawal or limitation of medical treatment	32	58	30	49	28	65
Brain death	30	23	24	22	38	17
Failed cardiopulmonary resuscitation	38	19	46	29	34	18

the doctors can take part in the removal of organs for transplantation.

The death of a child is traumatic. It is important that consistent terms are used to convey information about death to a family. Euphemisms should be avoided. I prefer to say that the child has died, rather than using the terms "brain death" or "brain stem death."

If possible, the issue of organ donation should be discussed with the family. It can provide comfort for the parents of a dead child to be able to help families whose children would die without an organ donor.

When the cause of death is not certain, permission for an autopsy should be requested. This is especially important if an underlying genetic disorder is suspected. A definite diagnosis can help prevent the tragedy of subsequent children dying of a rare syndrome or metabolic disease.

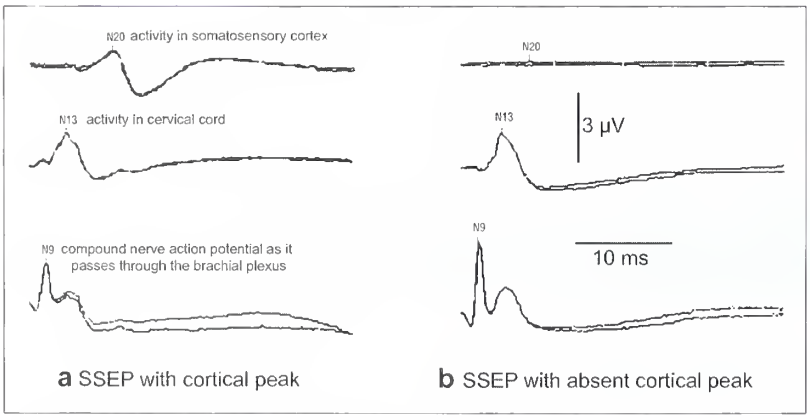
The child in permanent vegetative state

Permanent vegetative state can occur as a result of a variety of insults, such as hypoxia or trauma. The child is totally dependent on others for all aspects of care and does not react to, or interact with, the outside world. One test result that has been found to be of great value in giving a prognosis of, at best, permanent vegetative state in comatose patients is absence of cortical peaks in the somatosensory evoked potential (SSEP).[8,9]

The SSEPs are produced by stimulating a peripheral nerve with a brief electrical pulse. The median nerve at the wrist is often used. The responses are recorded at sites specified by a standardized plan (the International 10-20 System). Diagrams of present (a) and absent (b) cortical peaks are shown in the figure.

Feeding, as well as medical treatment, is sometimes withdrawn from patients in permanent vegetative states. This raises emotional issues for the staff caring for the patient. Legal advice is usually obtained before such a course of action is undertaken. There is no legal precedent in the United States for withdrawal of feeding in a child in a permanent vegetative state.

The high-profile legal cases of Karen Ann Quinlan and Nancy Cruzan represent examples of withdrawal of support in adults in vegetative states. No statistics are available on how often such a decision is quietly agreed on by the parents and physicians of a child in such a condition.



Somatosensory evoked potentials of a peripheral nerve showing (a) a cortical peak and (b) absence of a cortical peak, indicating a possible permanent vegetative state. SSEP = somatosensory evoked potentials

Case History

Michael was a 4-year-old boy who was found at the bottom of a swimming pool. Cardiopulmonary resuscitation was started at the scene and was continued in the local emergency department where he was intubated. A heartbeat was established after 3 rounds of medication.

Michael required high ventilator settings. Over the next week he had sluggishly reactive pupils and corneal reflexes, but did not show any purposeful response to stimulation. SSEPs on 2 occasions showed absent cortical peaks. A family conference was held. It was explained to his family that, at best, Michael would live the rest of his life in a permanent vegetative state. After meeting with their minister, Michael's parents agreed to extubation. He died 30 minutes later.

The "no chance" situation

The "no chance" category covers the child for whom life-sustaining treatment will merely delay death, without significantly relieving the suffering caused by the disease.

Case history

Sarah was a 5-year-old girl with acute myeloid leukemia. The intention had been to perform bone marrow transplantation after chemotherapy had induced remission. She tolerated treatment poorly, developing sepsis and difficulty breathing. She was intubated and transferred to the pediatric intensive care unit, but her condition continued to deteriorate. She required progressively increasing ventilator settings. She had completed her course of chemotherapy, but a peripheral blood smear still showed blasts, indicating active leukemic disease. A family conference was held. Her parents agreed that the current therapy should be continued, but it should not be escalated. They did not want cardiopulmonary resuscitation to be performed in the event Sarah had a cardiac arrest. Four days later, Sarah's heart went into asystole. In accordance with her family's wishes, she was not resuscitated.

It is important to document in the patient's notes what is discussed at a family conference. Therapy tends to progress in its degree of invasiveness, and specific information should be conveyed to all staff regarding the plan for interventions such as use of antibiotics to treat infection, cardiopulmonary resuscitation, and mechanical ventilation.

The "no purpose" situation

"No purpose" refers to when a child's life may be saved by medical treatment, but the degree of mental or physical impairment may be so great that the quality of life for the child is intolerable. This is probably the category in which conflict between the family and medical staff is most likely to occur, as was recently demonstrated in the United Kingdom by the case of David Glass, a 12-year-old boy with spastic quadriplegia and blindness. When David developed a serious chest infection in October 1999, medical staff at St Mary's Hospital, Portsmouth, administered only palliative treatment. Police were called to the hospital when family members struggled to resuscitate the boy. His mother failed in her Court of Appeal attempt to prevent doctors from refusing life-saving treatment for David without first obtaining a court order.[10]

The UK's Court of Appeal in 1991 recognized that a quality of life that may be considered intolerable to an able-bodied person would not necessarily be unacceptable to a child born with a disability.[11] In her book *I Know Why the Caged Bird Sings,* Maya Angelou notes that "children's talent to endure stems from their ignorance of alternatives."[12]

The degree to which altered awareness and inability to interact with family and the environment constitutes an intolerable handicap needs to be explored carefully with all those involved with the child. This should include the primary care physician and the family.

Case history

Jimmy was a 12-year-old boy with spastic quadriplegia from cerebral palsy. He was admitted to the surgical service with a rigid abdomen and appeared to be in severe pain. His mother reported that he had not had a bowel movement for a week. An abdominal radiograph showed air under the diaphragm. It was thought that Jimmy had a perforated colon. The surgical team was concerned that his frail condition might preclude his recovery and discussed with his mother the option of palliation of his pain with an opioid infusion, foregoing surgery.

Jimmy's mother felt that he did not appear more ill than he had 2 years ago when he was admitted to the hospital with severe constipation. She described that despite his handicaps, Jimmy enjoyed being held and talked to, he loved music, and he giggled at jokes. She realized that he might not survive major surgery, but wanted his life to be saved if possible.

An exploratory laparotomy revealed a perforated gastric ulcer. Jimmy had no postoperative complications. His constipation was treated, and he was discharged after a week. When he was being wheeled out of the ward, to everyone's amazement he clearly said, "home." He had not spoken during his hospital admission.

In most families, severely handicapped children are cherished as much as their normal siblings. Unless a poor prognosis is certain, and medical intervention burdensome to the extreme, the family's wishes for treatment should be respected.

The "unbearable" situation

In the face of progressive disease, additional treatment may only cause further suffering, despite the possibility that it might have some potential benefit on the underlying condition. Children with cancer may fall into this category. The wishes of the child as well as the parents need to be taken into consideration. Adolescents and younger children may have their awareness of death accelerated by their illness and can have a clear idea of the acceptability of the burdens of treatment and its possible benefits.[13]

After the decision has been made to withdraw or withhold further treatment, expert palliative care must be provided. Wolfe found that in pediatric oncology patients in whom curative treatment had been discontinued, the majority had uncontrolled pain and other symptoms before their death.[14] Pediatric hospice teams provide expert palliative care and should be consulted before the child has uncontrolled symptoms. In California, a new law (AB 791) mandates medical schools to teach students about pain management and end-of-life care.

TELLING THE FAMILY ABOUT WITHDRAWAL OF SUPPORT

In the pediatric intensive care unit at Mattel Children's Hospital of the University of California at Los Angeles, family conferences are used to convey updates on a child's condition and to discuss treatment options and prognosis.

Barry Beckham

The decision to withdraw support of a child can be a lonely one for parents

Barry Beckham

The death of a child is traumatic for both the family and the medical staff

These meetings typically include the unit consultant, the junior doctor caring for the child, the primary nurse, and the clinical social worker, together with the neurologist or other specialists involved in the child's care. Ideally, the child's primary care physician also attends. Prior to meeting with the parents, all those participating in the care of the child have an opportunity to voice their opinions and feelings. The parents and other close family members then enter. If necessary, a hospital interpreter is employed rather than relying on 1 of the family members to translate.

After introductions are made, the parents are asked about their understanding of the child's condition. This enables the staff to gauge how much information needs to be transmitted and how this should be done. Significantly different language and concepts may be needed for parents who left school at the age of 14 compared with those who graduated from university.

Patience and gentleness are essential when giving parents news of the inevitability of a poor prognosis. It is rare that just 1 meeting is sufficient for a family to accept a child's death and to agree to withdrawal or limitation of support. Great sensitivity is needed on the part of the physician chairing the family conference to pace the amount of information given. There should be no impression of rushing the parents, and conversely, the decision to withdraw or withhold support should not be postponed indefinitely.

Although paternalism is out of favor in medicine today, the burden of the decision to withdraw support from their child is a heavy one for parents to bear. The physician can emphasize that the medical staff are making the recommendation. It is a disservice to present all technologically feasible options to the family and then offer to do whatever the family wants. Nelson refers to this as "vending machine medicine."[15]

Although dissent by the parents rarely becomes an issue in the decision to withdraw support, the following steps can be taken if this arises. The medical staff can try to explore the reasons parents want to pursue treatment. There may be issues of guilt involved, which could arise when the child has a genetic disorder or has been involved in an accident for which the parent feels responsible. Religious beliefs may make the family feel that they have to keep their child alive irrespective of the underlying medical condition. Involvement of the family's religious leader can be helpful. It is often comforting to the family to have a religious ceremony at the child's bedside.

Obtaining a second opinion can be helpful, with the expert coming from an outside institution if necessary.

Most hospitals have an ethics committee to which difficult cases can be presented, usually after the family conference. Both medical staff and families should be able to obtain support, particularly by the formal acknowledgement of the committee of the complex issues involved.[16] The Royal College framework cautions that an ethics

Resources

The Compassionate Friends
PO Box 3696
Oak Brooke, IL 60522-3693
Phone: (800) 448 4570
Phone: (630) 990 0010
Fax: (630) 990 0246
www.compassionatefriends.org
nationaloffice@compassionatefriends.org
Bereavement support for parents

National Organization for Rare Disorders (NORD)
100 Route 37
PO Box 8923
New Fairfield, CT 06812-8923
Phone: (800) 999 6673
Fax: (203) 746 6481
www.nord_rdb.com/~orphan
orphan@rarediseases.org
Acts as a clearing hause for families with rare disorders

End of Life Physician Education Resource Center (EPERC)
Medical College of Wisconsin
8701 Watertown Plank Road
Milwaukee, WI 53226
Phone: (414) 456 4353
Fax: (414) 456 6506
www.eperc.mcw.edu
eperc@mcw.edu
Assists physician educators and others in locating training materials

committee may be too remote from the case to understand all of its aspects.[7] Ethics committees almost always provide consultation rather than a binding decision.

If conflict between the medical staff and parents cannot be resolved, the courts remain the last option. In the United Kingdom, the official solicitor's office can be telephoned for advice. A hearing generally takes place in High Court, at which the parents must be able to express their own concerns. Fortunately, such stalemates between parents and medical staff are extremely rare.

AFTER A CHILD HAS DIED

The death of a child is 1 of the most painful grief experiences imaginable. Bereavement care is important for the parents and siblings. A meeting with the family several weeks after the child's death can provide the opportunity for questions to be answered, particularly if an autopsy was performed. It also allows evidence of pathological grief reactions to be evaluated. Referral to such groups as the Compassionate Friends can be made (see box).

CONCLUSION

In pediatric care, there are a number situations where continued curative treatment is either futile or causes unacceptable suffering to the child. The decision to withdraw support requires effective communication between the hospital staff and the child's family. After treatment aimed at cure has been withdrawn, palliative care and emotional support are essential.

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COMMENTARY

Withdrawing and withholding life-sustaining treatment in children

The decision to withhold or withdraw life-sustaining treatment from a child is always a difficult one. As health care professionals and parents seek to do what is best for a child, they may face the difficult challenge of determining when the benefits of a medical treatment no longer justify the burdens imposed on the child. Tournay discusses a practice framework published by the Royal College of Pediatrics and Child Health (RCPCH) to identify circumstances in which intensive treatment may not be in the best interest of the child. Her discussion includes several helpful observations to assist the clinician in avoiding conflicts with parents over these issues.

Withdrawing or withholding life-sustaining treatments may be ethically justified when doing so best serves the interests of the patient. If the patient is competent to make medical decisions and has made her wishes known, those wishes should be respected. The law does not recognize children as competent to make medical decisions until they reach a certain age (18 years old in most states). However, adolescents are often capable of understanding the consequences of their decisions, may have given serious thought to what interventions they would consider to be excessive, and may be competent to make complex decisions about their medical care. When possible, these adolescent patients should be included in decisions regarding their care and have their wishes respected.

In situations where the patient is not competent to make decisions about his or her medical care, the decision to withdraw or withhold a given treatment modality may be justified when the burdens and harms of the intervention exceed any potential or actual benefits to the patient. The RCPCH framework suggests 5 circumstances in

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None declared

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which aggressive medical intervention ceases to be in the best interest of a child. Brain death and permanent vegetative state are 2 situations in which a child can no longer appreciate benefit from any therapy, and life-sustaining interventions, therefore, may be justifiably discontinued. The "no chance" situation, the "no purpose" situation, and the "unbearable" situation are all examples of situations in which the burdens and harms of continuing a therapy frequently exceed any benefit or potential benefit the therapy might offer.

It is important to note, however, that the determination of what constitutes a no chance, no purpose, or unbearable situation may be a matter of legitimate dispute. Tournay illustrates this important truth in her discussion of a no purpose case in which quality of life becomes a point of contention. While a decision to withdraw ventilator support or withhold antibiotics certainly has medical and scientific dimensions, values are inherently enmeshed in these decisions. Burden and benefit are not easily quantified concepts, and different people will come to different conclusions about what is best or unbearable or without purpose in a given situation. Because most decisions to discontinue or withhold aggressive medical interventions in a critically ill or dying child ultimately involve an assessment of what is best for that child—an assessment that involves a weighing of values—health care professionals should not impose a decision in the face of parental dissent. The goal is collaborative decision making with the welfare of the child at the center of the discussion.[1] Justice requires that in situations of intractable disagreement, institutional procedures (like an ethics consultation service) exist for the fair resolution of conflicts.

Children will sometimes die despite our best efforts, and we run the risk of compounding that tragedy when we lack the courage and wisdom to recognize the limits of our technology. A misguided effort to "save" a child can easily rob her of the opportunity to be touched and cared for by those she loves, to say goodbye, and to be held by those who love her without the distraction of overly burdensome interventions. We can too easily forget that the patient and not the disease is the object of our care. Stanley Hauerwas has perhaps said it best: "The great art of medicine is to care for them even when you cannot cure them."[2]

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The cardiac complications of recreational drug use

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INTRODUCTION

The use of recreational drugs has reached epidemic proportions in many countries and threatens to overwhelm economic, social, and health care systems. It is estimated that almost 1 in 4 people in developed countries have used recreational drugs at some time during their life. It is therefore inevitable that many doctors will have to manage and treat the ill effects associated with the abuse of these drugs.

In addition to their effects on the central nervous system, many of these agents induce profound changes in the heart and circulation that are responsible for a significant proportion of drug-related morbidity. This article reviews the cardiovascular complications associated with some of the commonly used recreational drugs.

METHODS

Data were obtained by electronically searching MEDLINE, Embase, Poisindex (Micromedex Healthcare Series 2000), and standard textbooks of pharmacology and toxicology. Specific drugs or their chemical names were used as the main search term.

Summary points

- The abuse of recreational drugs is common and it is inevitable that doctors will have to manage and treat their associated ill effects
- Recreational drugs are complex and can induce profound changes in cardiovascular function, both acute and chronic
- Recreational drugs are often taken together, which can result in complex synergistic interactions with potentially detrimental effects
- A high index of suspicion with early intervention and management is often the key to successful treatment

DRUGS AND SUBSTANCES

Cocaine, amphetamine, and ecstasy

Pharmacology

Cocaine, amphetamine, and ecstasy all share similar adverse effects on the cardiovascular system, related predominantly to sympathetic nervous system activation. Cocaine and its free-base form crack act by inhibiting the re-uptake of norepinephrine and dopamine at sympathetic nerve

terminals. Circulating catecholamine concentrations can be elevated as much as 5-fold in cocaine users.[1] At high doses, cocaine can impair myocyte electrical conduction and contractility.[1]

Amphetamine and its derivative ecstasy produce indirect sympathetic activation by releasing norepinephrine, dopamine, and serotonin from central and autonomic nervous system terminals.

Clinical effects

Sympathetic activation can lead to varying degrees of tachycardia, vasoconstriction, unpredictable blood pressure effects, and arrhythmias, depending on the dose taken and the presence or absence of coexisting cardiovascular disease.

Blood pressure changes

The high levels of circulating catecholamines and sympathetic activation commonly cause hypertension. However, hypotension can also occur (see box).[2]

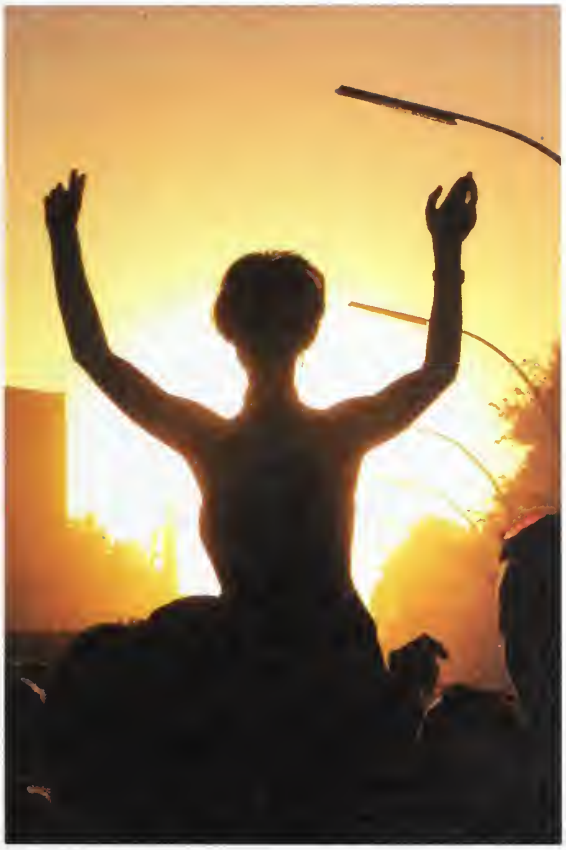
Suggested mechanisms by which cocaine, amphetamine, and ecstasy can cause hypotension

- Paradoxical suppression of the central sympathetic nervous system
- Relative catecholamine depletion
- Acute myocardial depression due to ischemia, direct toxic effect of the drug
- Mechanical complications, such as acute aortic rupture, tension pneumothorax, pneumopericardium

Myocardial ischemia and infarction

Cocaine and amphetamine can cause myocardial ischemia and infarction in patients with or without coronary artery disease. The mechanism is uncertain, but may be related to the elevated catecholamine concentration, which increases myocardial oxygen demand, coronary artery spasm, platelet aggregation, and thrombus formation.[2-4] Cocaine can produce a procoagulant effect by decreasing concentrations of protein C and antithrombin 3 and potentiating thromboxane production.[2]

Long-term use of cocaine and amphetamine can cause repetitive episodes of coronary spasm and paroxysms of hypertension, which may result in endothelial damage, coronary artery dissection, and acceleration of atherosclerosis.



Markus Schreiber

Recreational drug use has become more widespread

Aortic dissection, valvular damage, and endocarditis

Paroxysmal increases in blood pressure can lead to aortic dissection or valvular damage that increases the risk of endocarditis affecting mainly left-sided cardiac structures.[1] Endocarditis is often associated with unusual organisms such as *Candida, Pseudomonas,* or *Klebsiella* and frequently has an aggressive clinical course with marked valvular destruction, abscess formation, and a need for surgical intervention.

Cardiomyopathy

Prolonged administration of cocaine or amphetamines can also lead to a dilated cardiomyopathy.[2] Etiologic mechanisms include repeated episodes of subendocardial ischemia and fibrosis and myocyte necrosis produced by exposure to excessive catecholamine concentrations, infectious agents, and heavy metal contaminants (manganese is present in some cocaine preparations).

Pulmonary edema and pulmonary hypertension

Noncardiogenic pulmonary edema and pulmonary hypertension can also occur with cocaine and amphetamine misuse, although the precise underlying mechanism remains unknown.

Arrhythmias

The adverse cardiovascular changes and sympathetic stimulation associated with cocaine and amphetamine in-

gestion predispose to myocardial electrical instability, precipitating a wide and unpredictable range of supraventricular and ventricular tachyarrhythmias. The presence of fibrotic scars, myocardial ischemia, and left ventricular hypertrophy can act as a substrate for arrhythmogenesis. Cocaine possesses class 1 antiarrhythmic properties (blocks sodium channels) and can impair cardiac conduction causing prolongation of the PR interval, QRS complex, and QT interval. Cocaine can also cause a wide range of bradyarrhythmias, including sinus arrest and atrioventricular block.

Pneumothorax and pneumopericardium

Cocaine inhalation in association with a forced Valsalva maneuver (the positive ventilatory pressure increases drug absorption and therefore enhances the drug effect) can rarely give rise to a pneumothorax or pneumopericardium.

Lysergic acid diethylamide (LSD) and psilocybin ("magic mushrooms")

Pharmacology

Lysergic acid diethylamide (LSD) and psilocybin are commonly used hallucinogenic agents that are structurally related and have similar physiologic, pharmacologic, and clinical effects. LSD is about 100 times more potent than psilocybin. Their mechanisms of action are complex with various agonist, partial agonist, and antagonist effects at serotonergic, dopaminergic, and adrenergic receptors.[2]

Clinical effects

The adrenergic effects of these drugs are usually mild and can give rise to general sympathetic arousal leading to dilated pupils, tachycardia, hypertension, and hyperreflexia. Although cardiovascular complications are rarely serious, supraventricular tachyarrhythmias and myocardial infarction have been reported.[5] Changes in serotonin-induced platelet aggregation and sympathetically induced arterial vasospasm may have been contributory factors leading to the onset of myocardial infarction.[5]

Greg Smith/AP

Young people in nightclubs often take a cocktail of drugs and alcohol

Narcotic analgesics

Pharmacology

Morphine and its semisynthetic analogue heroin are the most commonly used recreational narcotic drugs. Narcotic agents act centrally on the vasomotor center to increase parasympathetic and reduce sympathetic activity.

Clinical effects

These autonomic changes, combined with histamine release from mast cell degranulation, can result in bradycardia and hypotension. Cardiac arrhythmias—including premature atrial and ventricular ectopic activity, atrial fibrillation, idioventricular rhythm, and ventricular tachyarrhythmias—have all been reported.[2] Bacterial endocarditis, affecting mainly right-sided cardiac structures, is a well-known complication of intravenous narcotic drug abuse, and it is sometimes associated with pulmonary abscesses. Heroin overdose can cause noncardiogenic pulmonary edema, the onset of which can be delayed for up to 24 hours after admission.[6] A disruption in alveolar-capillary membrane integrity has been suggested as a mechanism.

Volatile substance abuse

The abuse of volatile substances is an increasing problem among young male adolescents. The products used are legal, cheap, and easily available. Following inhalation, feelings of euphoria, excitement, and invulnerability can occur rapidly, but are short-lived.

Clinical effects

Cardiac arrhythmias are presumed to be the main cause of death from volatile substance abuse. Volatile substances may induce supraventricular or ventricular tachyarrhythmias by sympathetic activation or by myocardial sensitization to circulating catecholamines.[7] Some abusers spray the substances directly into the mouth, which can result in intense vagal stimulation and a reflex bradycardia. Profound bradycardia can evolve into asystole or secondary ventricular tachyarrhythmias. Some volatile compounds can reduce sinoatrial node automaticity, prolong the PR interval, and induce atrioventricular block.[2] Myocardial ischemia and infarction have been reported and are believed to be caused by a combination of coronary vasospasm, hypoxia caused by the formation of carboxyhemo-

globin or methemoglobinemia, or excessive sympathetic stimulation.[2] Long-term misuse can induce a poorly characterized cardiomyopathy.[8]

Cannabis

Pharmacology

Cannabis has a biphasic effect on the autonomic nervous system, depending on the dose absorbed.[3] Low or moderate doses can increase sympathetic and reduce parasympathetic activity, producing a tachycardia and an increase in cardiac output. In contrast, higher doses inhibit sympathetic and increase parasympathetic activity, resulting in bradycardia and hypotension. Reversible ECG abnormalities affecting the P and T waves and the ST segment have been reported.[9] It is not clear whether these changes occurred as a direct result of cannabis, independent of its effect on the heart rate.

Clinical effects

Although supraventricular and ventricular ectopic activity can occur, life-threatening tachy- or bradyarrhythmias have not been reported. In patients with ischemic heart disease, cannabis increases the frequency of anginal symptoms at low levels of exercise. This occurs as a result of a drug-induced increase in heart rate and myocardial contractility that increases myocardial oxygen demand.[2]

CONCLUSION

The abuse of illegal drugs is endemic in society and has the potential to cause major acute changes in cardiovascular function and irreversible damage to the heart. These drugs are frequently taken together as "cocktails," often in conjunction with alcohol. These combinations can have complex synergistic interactions, with potentially detrimental effects.

Many patients who present with complications will be unable or unwilling to provide a history of illegal drug use. Recreational drug use should always be suspected and looked for in patients presenting with unexplained or unusual cardiovascular disturbances associated with mood disturbances or central nervous system dysfunction. As drug misuse continues to permeate every level of society, it is inevitable that physicians will have to manage the devastating complications of these compounds. An awareness of the life-threatening cardiovascular effects, along with early diagnosis and intervention, is often the key to successful treatment.

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capsule

Students may delay putting on condoms One third of heterosexual students questioned about their use of condoms admitted that, on some occasions, they delayed putting on the condom until after initial penetration (*AIDS Care* 2000;12:221-224). Delayed use of a condom may have little influence on its contraceptive effect, but it may substantially reduce its effectiveness in preventing the transmission of disease. Studies of condom use need to take into account the possibility that people who claim they always use condoms may not do so from the start of coitus.

Correction

The picture accompanying Mary Ann Shafer's article in the November issue suggested that urine culture is being used in the diagnosis of chlamydial and gonococcal infections. In fact, non-culture nucleic acid testing of urine is being used to diagnose these infections.

Curbside Consult

Chronic fatigue syndrome: is it physical?

It is increasingly recognized that chronic fatigue syndrome (CFS) is heterogeneous. A significant proportion of patients fulfilling operative criteria for a diagnosis of CFS will also fulfill criteria for a psychiatric disorder, such as depression or somatization. Failure to recognize this heterogeneity prejudices attempts to understand CFS in cross-sectional studies.

Fulcher and White recently reported a study of muscle strength, aerobic exercise capacity, and functional incapacity in a group of patients with CFS without concurrent psychiatric disorder, compared with patients with major depression and a group of normal but sedentary subjects.[1] In an incremental treadmill exercise test, patients with CFS and patients with depression had lower peak oxygen consumption rates, maximal heart rates, and plasma lactate concentrations than the sedentary controls; but this reflected the shorter duration of exercise tolerated by these patients. At submaximal work rates, patients with CFS and depressed patients experienced greater perception of effort than sedentary controls at the same level of work. This is in keeping with the finding that such patients show greater sensitivity to bodily sensations than normal subjects.

Overall, there was little difference between the patients with CFS and the depressed patients in exercise characteristics, yet the patients with CFS reported significantly greater physical fatigue and physical incapacity. The authors did find one important difference, however. Their patients with CFS were significantly weaker than either the depressed patients or the sedentary controls, as judged by measurement of quadriceps strength. This is the first study to demonstrate such physical weakness in patients with CFS, and the authors suggest that this is because the patients they studied were more coherent than those studied previously.

Fatigue is a complex symptom. In its strictest sense, the word means "inability to sustain force," indicating dysfunction in the neuraxis or neuromuscular apparatus, whether physiologic (after strenuous exercise) or due to disease processes. In its colloquial context (*fatigare*—to tire), it is the sensation experienced when the effort to perform work, whether physical, mental, or both, seems disproportionate for the task involved. Physiologic fatigue recovers with rest. Chronic fatigue typically does not. Although chronic fatigue is a common complication of a wide range of medical and neurologic diseases, such as multiple sclerosis and Parkinson's disease, it can also occur in the absence of readily definable disease, notably in CFS.

What is the cause of this physical weakness in CFS? Fulcher and White think that it is related to physical deconditioning due to inactivity, and this view is supported by improvement in well-being, strength, and exer-

PR NewsFoto

People with chronic fatigue syndrome show measurable muscle weakness

cise capacity after a graded aerobic exercise program.[2] However, graded exercise therapy improves tolerance and exercise capacity in many disorders, including muscle diseases such as mitochondrial myopathies.[3]

Some patients with CFS show abnormal increases in plasma lactate levels after exercise at low work rates.[4] Heart rate responses to exercise in the 1995 study did not suggest that these patients with CFS were more "deconditioned" than those with normal lactate responses. They also proved less likely to have psychiatric disorder. Furthermore, recent spectroscopic studies of the forearm muscles, which are not usually subject to the effects of deconditioning, showed abnormal muscle energy metabolism in such cases.[5] Deconditioning may well be an important factor in the pathogenesis of CFS, but these findings raise the possibility that some patients with CFS have a form of metabolic myopathy.

Whatever the mechanisms underlying "fatigue," exercise therapy is likely to become an increasingly important therapeutic modality in various fields and particularly in the management of chronic fatigue syndromes.

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Culture and Medicine

Hospitals in rural America

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Summary points

- The role and structure of rural hospitals is changing, but they continue to be important local and regional centers of health care activity
- Rural hospitals tend to depend more on Medicare and Medicaid patients
- Most rural hospitals are organized on a not-for-profit basis
- Rural hospitals make an important contribution to rural economies; expansion and diversification of the services that they offer will be important in their survival
- The quality of care provided in rural hospitals is generally equal to that provided by urban institutions, with some exceptions

INTRODUCTION

The role of hospitals in the American health care system is changing rapidly, and some believe that hospitals may be replaced by networks of professionals and institutions tied together to coordinate care and promote health—the so-called virtual hospital. For many rural communities, however, the hospital has been the most effective form of health care delivery in the community.

In the 1980s, as the number of rural hospitals closing their doors grew every year, expert observers of the health care sector believed that rural hospitals were perhaps an anachronism and that only those institutions that were large and integrated with other parts of the health care system would survive.[1,2] The leading proposals for national health care financing reform from the White House and Congress in 1993 and 1994 did not provide much comfort for rural hospitals. By 1997, the reality of market changes overtook policy proposals; vertically integrated networks were a growing phenomenon, and the cost-saving potential of managed care was being realized.

Rural hospitals have survived in the present system partly because Medicare payment policies that were discriminatory to rural hospitals have been blunted by legislation and partly because there was a justification for the location and mission of hospitals in rural places. The number of closings dropped dramatically in 1994, and the dominant theme of rural hospital activities in the last half of the 1990s has been adaptation and innovation to meet the challenges of a changing market. Factors such as the rapid diffusion of new management techniques and the adoption of new structures and approaches to health care delivery have enabled rural hospitals to continue in their role as the local and regional centers of health care activity.

This article reviews the numbers, types, and structure of rural hospitals; describes their ownership and control; considers strategies for their survival; and discusses whether the quality of care that they provide equals that provided by urban institutions.

RURAL HOSPITALS: THEIR NUMBERS AND DISTRIBUTIONS

In early 1998, 2,182 nonfederal, acute-care general hospitals in nonmetropolitan counties made up 45% of the 4,821 hospitals total (figure 1). The nonmetropolitan hospitals are smaller: 72% have fewer than 100 beds, and 42% have fewer than 50 beds. Twenty percent of all hospital beds are in rural hospitals. The median number of staffed beds for nonmetropolitan hospitals is 59 compared with 156 for urban hospitals, while the average number of beds per hospital is 82 and 245, respectively. Rural hospital inpatient days account for 20% of all hospital inpatient days in the United States. Medicare and Medicaid are important sources of payment for hospital patients.

While there are substantial variations in hospital dependence on Medicare payments, rural hospitals tend to depend more on Medicare and Medicaid patients. Medicare pays for almost half of all rural hospital discharges compared with 37% for metropolitan hospitals. However, urban hospitals have higher use by Medicaid patients: 27% of all urban hospital days are for Medicaid patients while only 17% are for rural hospitals.

The use of urban and rural hospitals differed in 1996; urban hospitals had higher occupancy rates, but shorter lengths of stay (figure 2)

The distribution and characteristics of rural hospitals varies by geography—larger communities are much more likely to have a hospital than smaller communities.

OWNERSHIP AND CONTROL OF RURAL HOSPITALS

Hospital ownership and control are increasingly of interest to policy makers. The majority of rural hospitals are government-owned or fall under some other nonprofit classification; urban hospitals are predominantly owned by some other public sector entity that may not be a formal part of local government. A larger proportion of rural hospitals (23%) are contract-managed, compared with only 7% in urban areas. The type of government control can range from county to regional authority to state. More than twice the percentage of nonmetropolitan hospitals are controlled by government than are metropolitan hospitals (table 1). The number of nonmetropolitan hospitals that are organized on a for-profit basis is less than one-fourth that of metropolitan hospitals.

Of hospitals controlled by some government agency, county government and hospital districts account for the large majority of sponsors (figure 3).

RURAL HOSPITAL SURVIVAL

Between 1980 and 1998, there was an 11.8% decrease in the total number of community general hospitals due to closings, mergers, and conversions. The hospitals most vulnerable to closing or conversions were those that had fewer beds, had lower occupancy rates, were more often managed as a for-profit concern, were less likely to be accredited by the Joint Commission on Accreditation of Health Care Organizations (JCAHO), and had a high percentage of Medicaid inpatient days.[3] Among isolated hospitals, those in markets with higher population density were also more likely to close.[4] Studies that examined the effects of closed hospitals on local communities found significant changes in utilization, and in one case, health status.[5-7]

Economic contribution of rural hospitals

One of the key arguments in support of the continued subvention of rural hospitals by government and the removal of differential reimbursement rates for rural hospitals, is their contribution to overall rural economies. Doeksen, Christianson, and others have shown that rural hospitals contribute significantly to local economies and that rural hospitals serve as a source of employment and act as economic engines for many rural communities.[8-11]

Rural hospitals are often the largest or second largest employer in the towns where they are located, and they are an important part of the social capital of any community. The immense efforts taken by some communities to keep their hospitals open and operating is a measure of the great value people and communities place on a hospital.[12]

Strategies for rural hospital survival

During the period 1994 through 1997, a total of 28 rural hospitals closed, an average of 7 a year. Rural hospitals, like their urban counterparts, began to adapt to new market realities, including the need for greater accountability under managed care and the need to use available resources more efficiently. Studies of the strategies rural hospitals used for survival showed the importance of local resources, especially income-generating characteristics of the community, including the relative wealth of the population, employment patterns, and state-level policies that supported the hospitals.[12]

It is clear from the analysis of hospital survival that the conditions that confront the smallest rural hospitals are fundamentally different from what other hospitals experience. This is reflected in the recent development of policy to support alternative hospital structures and designs, including the Medical Assistance Facility, the Rural Primary Care Hospital, and the Critical Access Hospital. Management strategies for survival have varied, and there is no single, preferred blueprint for success for administrators.[13] However, there are abundant models of innovation and partnering[14] and of successful integration into networks[15].

There are many examples of communities banding together to save their small, rural hospital, but to be saved, many of the hospitals had to change. The options for change were once limited because of strict license and payment rules from Medicare and state Medicaid agencies. Since the mid 1980s, those options have expanded,

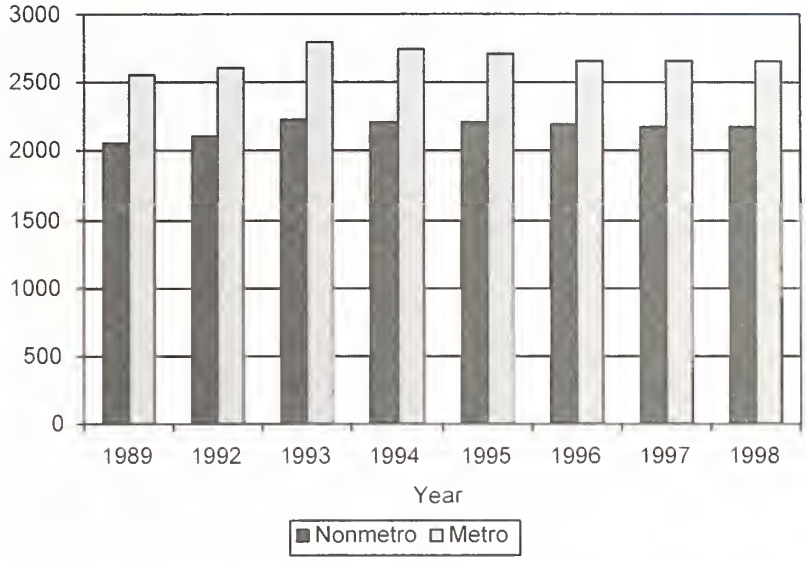

Figure 1 Number of nonmetropolitan and metropolitan hospitals, 1989-1998. (Source: Data from Annual Hospital Surveys for 1989–1998. Chicago: American Hospital Association. Ricketts TC, Heaphy P. Rural acute care hospitals that closed, 1991–1998. Chapel Hill, NC: Rural Health Research Program, Cecil G Sheps Center for Health Services, 1998.)

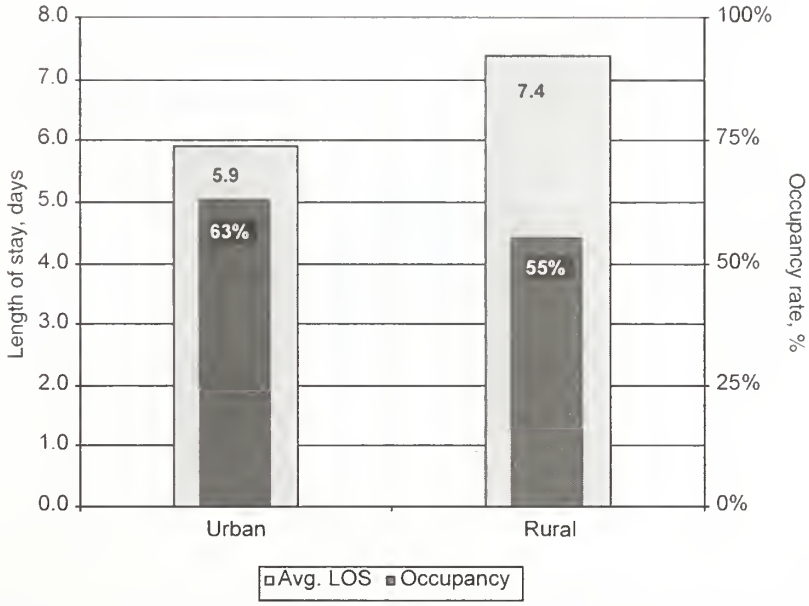

Figure 2 Hospital occupancy rate and average length of stay: urban and rural hospitals, 1996. LOS, length of stay. (Source: 1997 Annual Survey of Hospitals. Chicago: American Hospital Association.)

Table 1 *Hospital ownership and control, 1996*

	Number (% of total) Metro	Nonmetro
All hospitals	4018 (62.3%)	2430 (37.7%)
Hospitals controlled by		
Government	880 (21.9%)	1,110 (45.7%)
Church	447 (11.1%)	160 (6.6%)
Other nonprofit	1,740 (43.3%)	939 (38.6%)
For profit	951 (23.7%)	221 (9.1%)

Source: 1997 Annual Survey of Hospitals. Chicago: American Hospital Association.

both for vehicles to finance hospitals beyond the traditional corporate, nonprofit foundation, and authority structures, as well as in the forms that hospitals can take as they adapt. The organizational forms that are possible can be described in a matrix that scales the operational autonomy against the range of services offered at the facility (figure 4).

The options shown in figure 4 include affiliations that may expand or reduce the number of services offered at the facility while it remains an acute-care general hospital. Rural hospitals are flexible and can expand and diversify the service they offer to meet local needs for long-term care and specialized services.

Options for conversion include modifying the facility so that it ceases to be a hospital and becomes a primary-care center or an outpatient facility that specializes in surgery or diagnostic and evaluation activities. Many rural hospitals have converted to long-term care facilities because the existing physical structure allows for this modi-

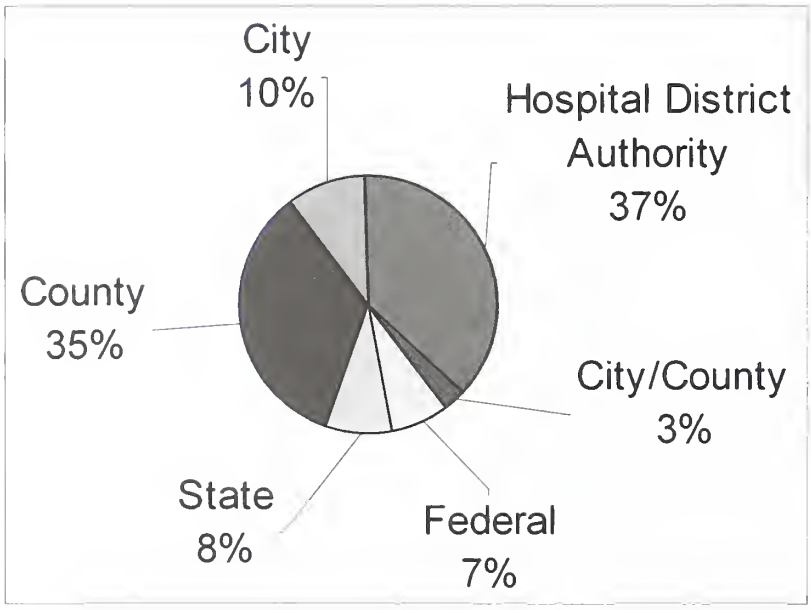

Figure 3 Type of control of public nonmetropolitan hospitals (Source: 1996 Annual Survey of Hospitals. Chicago: American Hospital Association.)

Douglas Dickema

Diversity: The approach in Prairie Du Chien, Wisconsin

Prairie du Chien Memorial Hospital, located in a community of 6,000 in Wisconsin, presents a case of an innovative hospital whose success can be attributed to its ability to do just about everything. This Crawford County hospital has a $6.5 million surplus and a 15% operating margin. The hospital has 44 beds, 22 of which are long-term care beds, and offers not only emergency, acute, and skilled nursing care, but also respite care, home health, durable medical equipment, home oxygen, and rehabilitation services. It has even expanded beyond providing just hospital-related services and now delivers meals to home-bound elderly people, operates a senior meal site in its cafeteria, manages an assisted living complex for seniors, operates a day care center, and contracts with the local prison to provide linen service and meals. "With all of these services, many of which are private pay, we can spread our overhead and be very efficient," says CEO Harold Brown. "[And] except for the assisted living, none of this takes a lot of capital." The multiple programs have created spin-off effects: The older people who come for lunch at the cafeteria will visit inpatients, and the drivers who deliver meals to people at home check on them and report problems. Such an arrangement demonstrates the success of a diversification scheme that not only provides more services, but also brings together the community citizens.

Source: Ready or not: rural hospitals are changing. Rural Health News 1997;4.

fication. Conversion is one option that can keep the organization running and the community presence alive.[16] However, the loss of emergency or obstetrical services, core components of a "real hospital," may force people to travel outside the community for some health care services.

Rural hospitals have been able to reconfigure their structures to provide a broader or more appropriate mix of services; some have converted many or all of their beds to long-term care while others emphasize outpatient care. Networks have been created among rural hospitals, or affiliations have been established with larger hospitals, physician groups, or other health care providers. In each case, the ultimate goal is to meet market needs and ensure institutional survival.

Douglas Dickema

QUALITY OF CARE

The quality of care provided in rural hospitals has generally been accepted as equal to that provided in urban institutions, with some exceptions. A controversial article by a team of R and investigators brought the issue of quality in small rural hospitals to the attention of a wider group of researchers.[17] The US Agency for Health Care Policy and Research contracted for a careful review of the evidence for whether low volumes and other characteristics of small, rural hospitals might affect patient outcomes.[18] The study found strong evidence of a volume-outcome effect for a certain set of conditions and

Clinical care program improves provider coordination and patient care

Rutland Regional Medical Center is a 188-bed hospital that serves a 6-county region in rural Vermont. In 1993, personnel at the hospital decided to assemble a working group to focus upon the ongoing problem of long lengths of stay. After looking at the multiple factors that affect patient outcomes and utilization—patient, nursing, physician, organizational, and environmental characteristics—the team decided to focus upon improving the clinical coordination of care. Their solution was to establish a Clinical Care Coordinator Program headed by "super nurses." The goal of the program was to facilitate patient care, increase the efficiency and communication of medical teams, and implement the continuous quality improvement process. At the end of 1 year, it was determined that not only had length of stay decreased significantly, but the medical staff was able to conduct rounds more smoothly, and patients and family members liked the access to a specific person who would listen and answer questions. Positive effects of the program include enhanced problem identification, improved communication, and increased patient satisfaction. The success of the program has not only improved the quality of care at Rutland Regional Medical Center, but has lead to its replication in the orthopedics service and community cancer center.

Source: Winstead-Fry P, Bormolini S, Keech RR. Clinical care coordination program—a working partnership. *J Nurs Adm* 1995; 25:46-51.

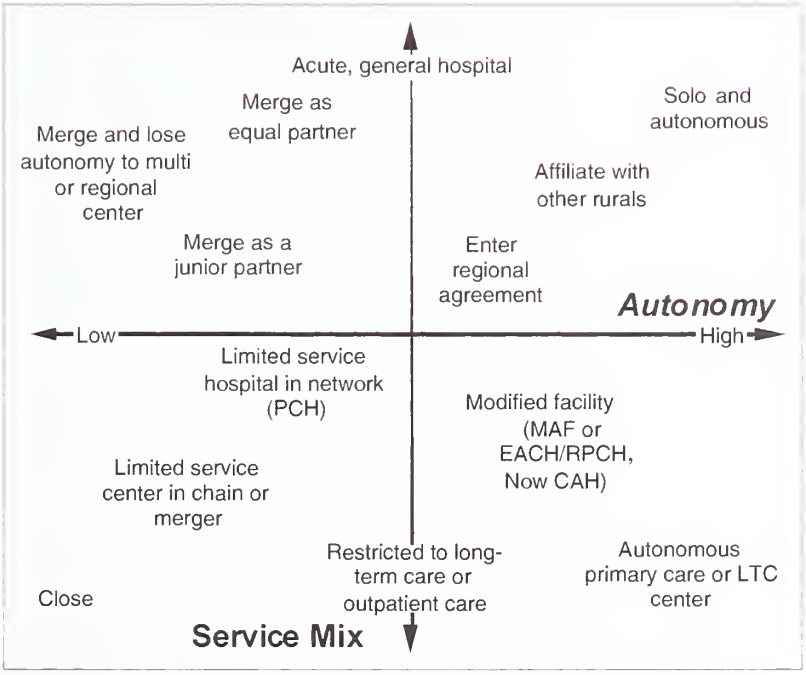

Figure 4 Strategic options for rural hospitals (Source: *Rural Health News* 1997:4.) PCH = primary care hospital; MAF = medical assistance facility; EACH/RPCH = essential access community hospital/rural primary care hospital; CAH = critical access hospital; LTC = long-term care.

Table 2 *Rural hospital focus on quality and community health needs*

	% of total 1993	1996	% change
Work in concert to conduct a health status assessment of the community			
Nonmetro	53.0	78.0	25.1
Metro	61.4	83.6	22.1
Used assessment to identify unmet health needs, excess capacity or duplicative services			
Nonmetro	56.4	61.7	5.3
Metro	64.8	74.0	9.2
Used health status indicators to design or modify services			
Nonmetro	47.8	65.2	17.3
Metro	67.2	82.2	15.1
Share clinical and health information with cooperating organizations			
Nonmetro	47.2	61.8	14.7
Metro	65.5	78.6	13.1
Disseminate cost and quality to the community			
Nonmetro	40.7	48.1	7.4
Metro	48.6	64.5	16.0

Source: 1997 Annual Survey of Hospitals. Chicago: American Hospital Association.

procedures, with low volumes associated with poorer outcomes. However, most procedures for which a volume-outcome relationship has been demonstrated are not typically performed in small rural hospitals. The strongest relationship between volume and outcomes has been found for coronary artery bypass graft or open heart surgery; total hip replacement, intra-abdominal artery operation or resection; cardiac catheterization and angiography; and transurethral prostatectomy. All but the last procedure were unlikely to be carried out in small rural hospitals. The analysis highlights that many procedures and conditions commonly treated in rural and urban hospitals have not been studied for a volume-outcome effect and that all hospitals need to improve their assessment of their patient care quality.

Assessing quality of care, health outcomes, and provider performance is a growing area of health care. Some would say that it is becoming a common part of the health care system as reports of hospital and health plan performance are more commonly published and disseminated. The increasing interest in quality comes when many are concerned that managed care may adversely affect quality through its focus on controlling costs. Although there is very little research evidence to support this belief, it has become a motivating reason to move away from a health care system based almost completely on price. Some hospitals have adopted continuous quality techniques to improve care, while many others with small staffs and limited resources have found it difficult to support a full-time quality assurance program. In spite of these limitations, many rural hospitals are addressing the needs of the community and finding opportunities to improve quality of care. In 1996, 78% of rural hospitals reported that they had worked in concert to assess the health status of the community, while only 65% said that they use health status indicators to design or modify services. The overall trend is toward an increased focus on quality and community needs, yet rural hospitals lag behind their urban counterparts (table 2.)

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Medical Myth

Myth: identifying classic coronary risk factors helps to predict the likelihood of acute ischemia

Since the initial findings of the Framingham and other longitudinal studies, clinicians are well aware of the risk factors for the development of coronary artery disease: age, male gender, hypercholesterolemia, diabetes, smoking, hypertension, and family history of myocardial infarction.[1] It has become routine for physicians to identify these risk factors in patients presenting to the emergency department with signs and symptoms of acute cardiac ischemia. Moreover, emergency department clinicians are using the presence or absence of these "classic" risk factors in addition to clinical presentation and electrocardiographic (ECG) findings to make decisions regarding the ultimate disposition of these patients. In this manner, many clinicians routinely consider patients without coronary risk factors at low risk for acute coronary syndromes even when they present with chest pain.

But Selker et al have shown that using a patient's coronary risk factors in the emergency department setting does not improve a physician's ability to diagnose acute ischemia.[2] The confusion about the use of risk factors stems from a misinterpretation of their predictive value. The classical coronary risk factors have been repeatedly shown to increase the risk of ischemic heart disease in patients followed over many years. But in the acute setting, physicians need to obtain patient data that will predict the risk of acute cardiac ischemia and—even more importantly—the risk of adverse events during that particular encounter. Factors that predict the development of ischemic heart disease over years, rather than acute events, are not helpful in the emergency department or acute care setting, and they may be seriously misleading.

By obtaining clinical data and reports of classical coronary risk factors, Selker et al performed a prospective study to determine whether the presence of the classical coronary risk factors increases the likelihood of acute cardiac ischemia beyond that expected from clinical presentation and ECG findings. Over 5,000 patients were enrolled, and logistic regression was used to calculate the relative risk of each coronary risk factor in predicting acute ischemia. They found that in men presenting to the emergency department with signs and symptoms of acute ischemia, the relative risk of cardiac ischemia for each classic risk factor was as follows: hypertension 1.0 (95% confidence interval [CI], 0.7-1.0), diabetes 2.4 (95% CI, 1.2-4.8), cigarette smoking 1.5 (95% CI, 1.0-2.4), and family history of myocardial infarction at younger than 50 years 1.5 (95% CI, 0.7-2.8).

In contrast, the relative risk of acute ischemia in patients complaining of chest pain was 12.1 (95% CI, 5.3-27.6), and in those with ischemic ECG changes it was 8.7 (95% CI, 5.0-14.8). The 1.5- to 2-fold relative risk of acute ischemia found in patients with diabetes and family history is extremely small in comparison. The study also found that in women, none of the classic risk factors increased the relative risk of acute ischemia beyond that of the history and ECG findings.

Goldman et al studied 10,000 patients with acute chest pain to identify possible clinical predictors of the development of major complications.[3] These factors included older age, male gender, pain similar to prior myocardial infarction, systolic blood pressure less than 110 mm Hg, and initial ECG changes.

CONCLUSION

The conclusion from these data is that clinical history and ECG findings are predictive of acute cardiac ischemia and

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Toby Talbot/AP

Classic coronary risk factors are not predictive of acute cardiac ischemia

risk of major complications, while classic coronary risk factors are not. Although the classic coronary risk factors may be part of a medical history, there is no evidence to suggest that they should be incorporated into the triage decision for a patient presenting with acute chest pain. The real concern is the prevalent myth that a lack of classic risk factors predicts a low risk of acute cardiac events in patients with chest pain. This myth may lead to inappropriate management decisions.

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Civilization and the colon

Constipation as "the disease of diseases"

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INTRODUCTION

The publication in April 2000 of the results of a clinical trial that found no protective effect of high-fiber cereal against colorectal adenomas stirred up considerable media attention and shook a cherished tenet of popular health culture.[1] After all, boxes of All-Bran cereal have been assuring us for nearly 2 decades that they contain "at last, some news about cancer you can live with,"[2] and the manufacturers of all bran cereals have enjoyed unprecedented profits, thanks to the assumption that their products ensure against colon cancer. What will happen to "the high-fiber feeding frenzy"[3] that has possessed Americans the past 20 years now that that assumption has been challenged?

Summary points

- Throughout human history, bowel irregularity has been considered dangerous to health
- 19th century medical scientists formulated a theory of "intestinal autointoxication," or self-poisoning from retained wastes
- The public became prey to marketers of anticonstipation foods, drugs, and devices—a bran cereal was introduced in the early 1900s to combat autointoxication
- Recent clinical evidence suggests that high-fiber cereal does not have a protective effect against bowel cancer
- Because constipation has a historic hold over the public mind, people may continue to believe that bran is protective

CONSTIPATION HAS ALWAYS BEEN FEARED

Not much, most likely. It is not just that the epidemiologists continue to remind us that there are many observational studies of population groups that show a correlation between consuming a bulky diet and a low incidence of colorectal cancer,[4] or that the gastroenterologic authorities continue to recommend daily ingestion of a minimum of 30 g of fiber.[5] More important than anything the experts have to say, I would wager, is human intuition, which has seen bowel irregularity to be dangerous from as far back as health literature can be traced. The oldest complete "book" in existence is an Egyptian pharmaceutic papyrus of the 16th century BC that offers as a basic explanation of disease the notion of poisoning of the body by material released from decomposing waste in the intestines.[6] The intuition was that disease is a process of internal putrefaction—as evidenced by the voiding of vomit, diarrhea, mucus, etc—and that that putrefaction can most easily be initiated by the contents of the colon, foul matter that is always undergoing a process of degeneration.

This compelling suspicion shaped medical theory for more than 3 millenia; the personal physician to France's Louis XV in the 18th century was merely echoing the Ebers Papyrus when he warned that disease was the result of blood turned "feculent" by contamination with "the depraved remains of concoction" in the intestines.[7(p21)]

From the late 1700s onward, European and American physicians were convinced that constipation was becoming ever more common because of changes in diet, exercise levels, and the pace of life associated with urbanization. By the beginning of the 19th century, there was a medical consensus that constipation was *the* "disease of civilization," a universal affliction in industrialized societies that engendered the full range of more serious human ailments. As a popular American health manual warned in the 1850s, "daily evacuation of the bowels is of the utmost importance to the maintenance of health"; without the daily movement, "the entire system will become deranged and corrupted."[8(p114)]

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CONSTIPATION AND THE GERM THEORY: "AUTOINTOXICATION"

Surely such simplistic pathology was consigned to the rubbish heap once the modern germ theory of disease came in during the last quarter of the 19th century. In truth, bacteriology only buttressed the ancient intuition that fecal decay triggers physical decay. The discovery that germs cause infection was an outgrowth of Pasteur's studies demonstrating that germs cause putrefaction of animal and vegetable material outside the body. The first practical application of Pasteur's findings, the introduction of antisepsis into surgery by Joseph Lister in the 1860s, further confirmed the germ-putrefaction connection; Lister employed a caustic chemical, carbolic acid, to suppress surgical wound infection because he thought of wound inflammation as a germ-induced putrefaction, and carbolic acid was known to inhibit putrefaction in sewage. But what was the colon if not a sewage pit teeming with bacteria, a cesspit that was not being sanitized with antiseptics nor, in the constipated, being regularly emptied? Might not its germ-infested foulness spread out somehow into the rest of the body?

A more elegant rationale for colonic corruption of the body became available in the mid-1880s, when bacteriologists came to realize that intestinal flora broke down protein residues in feces into several compounds that exhibited pronounced toxicity when injected into animals. Reasoning that putrescine, cadaverine, and similar "ptomaines" generated in the bowel could be absorbed into the bloodstream, late 19th-century medical scientists formulated the theory of intestinal autointoxication, or self-poisoning, from one's own retained wastes. The constipated person, French physician Charles Bouchard declared, "is always working toward his own destruction; he makes continual attempts at suicide by intoxication."[9(p15)]

Autointoxication not only bore the imprimatur of the most modern medical science, it met a clinical need to come up with an explanation and diagnosis for all those exasperating patients who insist that they're sick but are unable to present the physician with any clear organic disease. Thus, even though autointoxication was, to paraphrase Pudd'nhead Wilson, nothing more than constipation with a college education, it became its era's catchall diagnosis, the pigeonhole into which cases of headache, indigestion, impotence, nervousness, insomnia, or any number of other functional disorders of indeterminate origin could be placed. The diagnosis was not restricted to such relatively benign complaints, however, because heart disease, cancer, and other deadly ailments did not always have obvious causes either.

Given enough time, it appeared, toxins absorbed from the torpid bowel could wreak just about any degree of havoc anywhere in the body. Indeed, from 1900 into the 1920s, autointoxication was regarded by much of the medical profession and most of the public as the most insidious disease of all, because it was, in essence, all diseases. In books such as *The Conquest of Constipation, The Lazy Colon,* and *Le Colon Homicide,* physicians on both sides of the Atlantic warned that the contents of the colon were "a burden, fermenting, decomposing, putrefying, filling the body with poisonous substances" and creating "sewer-like blood"[10(p88)]; that autointoxication "is the cause of ninety per cent of disease," and that "constipation shortens life."[11(pp25,28)]

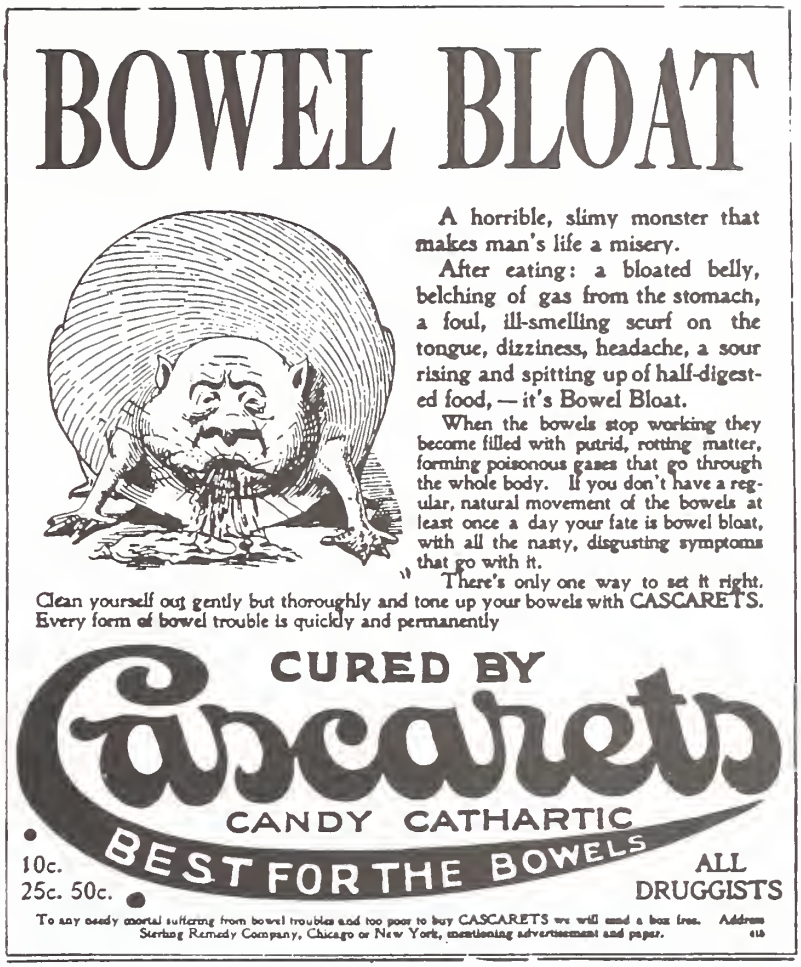

Figure 1 An advertisement for a "candy cathartic" (photo courtesy of the University of Washington Libraries, Special Collections Division, negative UW 17931)

PREVENTION AND TREATMENT OF AUTOINTOXICATION

Physicians were also generous with advice on preventing constipation, but recommendations to eat more fruits, vegetables, and whole grains, to be more physically active, and to always respond promptly to nature's morning call to evacuate seemed to many people to require more self-discipline and sacrifice than they cared to exercise. The autointoxication-anxious public thus fell easy prey to all

manner of marketers of anticonstipation foods, drugs, and devices. All-Bran cereal was introduced in the early 1900s precisely to combat autointoxication, as were many other bran cereals such as the not-so-subtly named DinaMite. Yeast was a heavily promoted dietary preventive of constipation, and yogurt acquired its reputation as a health food when recommended in the first decade of the century to forestall autointoxication.

Still more popular were laxatives. The 1920s and 1930s were the "golden age of purgation" as literally hundreds of brands of bowel cleansers competed for consumer dollars with lurid advertisements such as the Cascarets warning of the dangers of "bowel bloat" (figure 1). Phenolphthalein, introduced as a cathartic in 1900, quickly claimed the position of the best selling of all laxatives on the strength of its marketing campaign to rescue innocent children from the clutches of autointoxication. Indeed, the manufacturers of brands running from best-selling Ex-Lax to the onomatopoeic Zam Zam laid down a relentless advertising barrage aimed at frightening parents into giving their children daily doses of chocolate-coated or otherwise pleasantly disguised phenolphthalein, making it sound as if the chief source of pediatricians' income must be epidemic laxative deficiency.

A horde of device salespeople swept over the land as well, peddling an astounding collection of merchandise: enema and colonic irrigation equipment, abdominal support belts, abdominal massage machines (figure 2),[12(p281)] electrical stimulators, rectal dilators (figure 3), and on and on. Not the least intimidating of the cures for autointoxication was surgery—colectomy, to be precise—popularized by the renowned surgeon of London's Guy's Hospital, Sir William Arbuthnot Lane. Between 1900 and 1920, Lane extirpated the colons of hundreds of constipates, maintaining that his streamlining of the human "drainage scheme" was "the most satisfactory result of surgery known to us at the present time."[13]

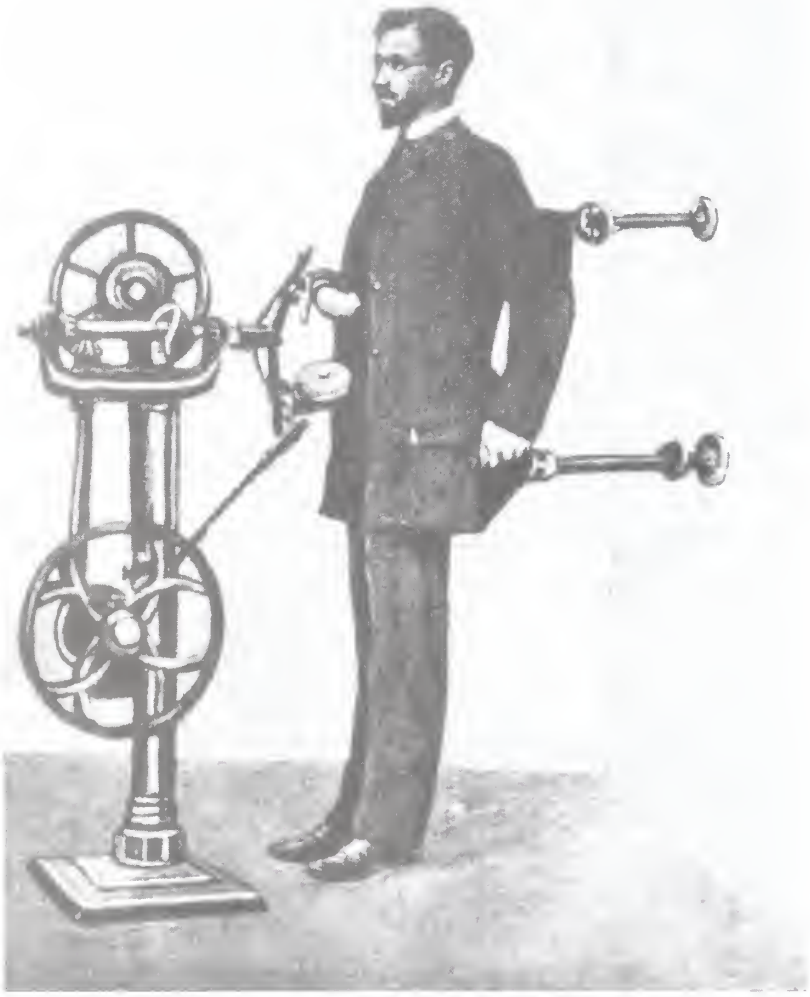

Figure 2 An abdominal massage machine (from Gant[12])

CONSTIPATION RELATED TO "CIVILIZATION"

A number of experimental studies in the 1910s cast doubt on the possibility of bowel toxins leaching into the circulation, and autointoxication slowly faded from professional acceptance during the 1920s. Fear of constipation continued to be exploited by laxative and other manufacturers, of course, but more pertinent was Lane's persistent belief in constipation as a disease exclusive to urban, industrial civilization—as, in fact, "the disease of diseases," as he dubbed it, "the cause of all the hideous sequence of maladies peculiar to civilization."[14] Lane had a distinctive theoretic argument for identifying constipation as a disease of civilization, explaining how the living habits of people in the developed world distorted the colon's anatomy in a way not suffered by "savage races."[15(pp36-37)] More important in the long run, however, was the epidemiologic justification for his contention that constipation was the true white man's burden. Although he did none of the sophisticated statistical comparisons of disease incidence in developed and undeveloped countries that became the norm in the second half of the 20th century, he read widely in the publications of European physicians practicing in India and in African nations and became convinced that both constipation and a number of ailments common to Europe and America existed at low levels among "uncivilized" populations. Lane was particularly adamant that colon cancer was rare in preindustrial peoples because their bowels moved frequently due to a diet of whole grain cereal foods: "the whiter your bread," he liked to say, "the sooner you're dead."[16]

THE DIETARY FIBER HYPOTHESIS AND "WESTERN DISEASES"

One sees in Lane the germs of the dietary fiber hypothesis and the concept of "western diseases" developed most notably by English surgeon Denis Burkitt in the 1970s and 1980s. Burkitt told me in conversation that he was unaware of Lane's work until he was well along in the formulation of his own ideas about fiber. Nonetheless, a link exists, as Burkitt was inspired by the "saccharine disease" theory of British naval surgeon T. L. Cleave, who drew on the observations of Sir Robert McCarrison, a British physician in India during Lane's day. McCarrison's reports of the rarity of colon cancer, appendicitis, and gastric and duodenal ulcer among the grain-eating Hunza of northern India were used by Lane as the cornerstone of his theory. Burkitt, too, saw that "constipation is the commonest western disease,"[17(p427)] and his exhortations to westerners to consume more dietary fiber to ward off colon cancer and other ailments of industrialized societies, an obituarist observed, "was to change the breakfast tables of the western world."[18]

CONCLUSIONS

I would guess that, given the historic hold of constipation on the public mind, most of those tables will stay changed no matter how many clinical trials deny that Burkitt and Lane were right about bran and colon cancer. People instinctively appreciate the wisdom of an elderly Scottish physician who used to consult with another Guy's Hospital surgeon, Sir Astley Cooper, in the early 1800s. "Weel, Mister Cooper," he would say just before entering the sick room, "we ha' only twa things to keep in meend, and they'll searve us for here and herea'ter; one is always to have the fear of the Laird before our ees, that ill do for herea'ter; and t'other is to keep your booels open, and that will do for here."[19(p18)]

James C Whorton is professor of the histoty of medicine in the Department of Medical Histoty and Ethics, University of Washington School of Medicine. His recent book, *Inner Hygiene: Constipation and the Pursuit of Health in Modern Society* (New York: Oxford University Press; 2000), examines American and British attitudes toward constipation as the fundamental "disease of civilization" over the past 2 centuries.

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Figure 3 Rectal dilators for the "relief of rectal irritation and itching" (from *Nature's Path,* December 1938)

Letter from Abroad

The power of song

Mary Clark, New York, NY
marydujour@aol.com
West J Med 2000;173:428-430

I am a theater artist, and for 7 years I ran a small touring company. We would develop and write our material; build costumes, wigs, puppets, and sets; arrange music; teach workshops; perform; and run the business. International festivals as well as elementary schools commissioned my work, which is based on European-style physical and visual theater. I also direct an a cappella harmony group. I love my work in the arts but have always felt that it is a luxury—entertainment for those who already have the basics covered.

I longed to be of practical service to people in need, so in 1998 I went to Swaziland for 2 months as a volunteer. The plan was for me to work with a small charitable organization delivering nutritional supplements, treatments for sexually transmitted infections, HIV education, and basic health care services to villages, clinics, schools, and church communities. I have no formal medical education—my background in health is limited to a strong foundation in anatomy, nutrition, and preventive medicine, the necessary tools for a healthy life without health insurance. In Swaziland, I would be the "gofer"—packaging mixtures of vitamin supplements, distributing water and green vegetables, and carrying heavy boxes—which, thanks to my arts work, I do very well and without complaining.

The mission of the organization was to teach about health matters in an attempt to bridge widening gaps in an overtaxed health care system. Swaziland, though blessed with peace and stable race relations, has a corn-

PK, the traditional healer, in his hut

Health care work in Swaziland

based diet high in sugars, a high prevalence of sexually transmitted infections, a growing rate of HIV infection, an explosion of orphans, and evidence of disease that no longer responds to treatment with antibiotics. The hospitals are painfully overcrowded, and terminally ill patients may be discharged from the hospital to make room for more treatable cases.

On my first day, we made the weekly visit to a clinic compound run by a traditional healer named PK. PK had built his clinic for poor villagers and patients considered by the hospital system to have an incurable condition. The clinic was a miniature village of huts busy with goats, dogs, children, and extended family members looking after sick relatives. PK had treatment rooms with running water, but the huts were simply shelters with cots or blankets on the floor. Indoor space was at a premium, with some huts overflowing.

I could smile and gesture to patients at the clinic, but my limited knowledge of Siswati, the native language, made communication difficult. On a visit near the end of my stay, Jane Cox, a Swazi health care worker and our translator, asked me to come to one of the huts. Five women shared it, and every inch of the hut space was taken up by a patient on a bed or a blanket. One of the women, Ida, was crying because she had just been told that she must go back to the hospital to have both legs amputated. As a double amputee, she would be unable to care for her children, grow crops, or tend the cattle. Ida was in despair. Jane asked if I would sing something for her.

Jane started to speak, and I assumed that she was telling the women that I was a singer at home and that I would like to sing for them. When she mentioned my name, Mary Clark, the women's faces lit up, and an older woman who appeared to be the grandmother shouted out, "Merry Christmas! Merry Christmas!" The women laughed and joined in with calls of "Merry Christmas, America" and "Hallelujah!" interspersed with Siswati. Then they were silent. Jane told me that they wanted to hear a song from my home. A million songs flew through my mind, and I tried to find one that they might connect to, even though I would be singing in a foreign language. Elvis and the Beatles are well known around the world, but these women would have had no radio exposure. But they did go to church, so I started a Patsy Cline favorite, "Just a Closer Walk With Thee." I saw their interest and appreciation but realized that "Jesus," a name they would recognize, was not mentioned much in the song. In an attempt to connect more strongly, I went straight from the verse I was singing to a chorus of "Glory, Glory, Hallelujah" from the "Battle Hymn of the Republic."

The women burst into song.

Ida rocked, cried, and sang; the grandmother's voice wailed "Hallelujah!" over the top of the other voices; and a woman with AIDS tried to lift her head from the pillow to join in. These frail bodies held voices of power and heart and sang for themselves, their families, their pain, their hopes, and their God. I knelt down to be at the same level as them, unable to stop my tears, and we finished out 3 choruses of "Glory, Glory," crying and applauding.

I asked Jane if they would sing a song for me. Jane asked them, and a woman holding a child led with a beautiful call, "Siyabonga Nkosi (We thank you, God)." Ida and her bedmate sat up, clapping and chiming out the 2-part syncopated response. The grandmother and I traded "Amens" and "Hallelujahs," and when we finished, they asked me to sing again. I offered a South African song, "Siyahamba," which they knew. Voices from around the compound started to sing, and for a moment I was part of a community joined in song.

When I left that day, I was both exhilarated and full of regret. I thought how ironic it is that it takes so much work, time, and effort for my US singing group to sing "well" together. And I thought of all that we had at home and that these women would never have. I did not want this moment of effortless harmony to end. The women waved goodbye but kept on singing. Four days later, I left the country.

Postscript

Jane contacted me a month after I left. Ida was healing and would not need the amputations.

My harmony group was invited to sing at the United Nations Commission on Sustainable Development. We were asked to sing songs of hope, justice, and inspiration in a high council chamber during the commission meeting—singing as part of the political dialogue. The organizers were nervous; to their knowledge, music had never before been presented in this way at the UN.

We sang 4 songs of different languages and cultures. The delegates were surprised and seemed touched by the music. For our last song, I moved forward and started to sing "Siyahamba." Instantly, delegates from all over southern Africa were leaping to their feet, singing out, and running to the center of the chamber to dance. Seconds later, everyone in the UN Council Chamber was up, swaying and clapping. There were delegates from all corners of the earth—heads of businesses and nongovernmental organizations—dancing with the simultaneous translators in their booths at the back. The nations seemed truly united, and for a moment, I was part of a community joined in song. Hallelujah.

Mary Clark creates community arts projects and teaches world harmony music. Jane Cox now runs the Moya Center, a free clinic and healing and arts center in the Ezulwini Valley in Swaziland. She can be contacted at mj.cox@africaonline.co.sz.

You can hear 2 songs recorded by sangomas—traditional South African healers—when you visit our website–www.ewjm.com.

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JANUARY 24-27, 2001: The Ninth Annual Medicine Meets Virtual Reality Conference: Outer Space, Inner Space, Virtual Space. Newport Beach Marriott Hotel & Tennis Club, Newport Beach, CA. Contact Aligned Management Associates Fax (760) 751-8842; jim@amainc.com.

JANUARY 24-27, 2001: 7th Annual Sports Medicine Conference. Providence Everett Medical Center at the Sun Mountain Lodge, Winthrop, WA. Contact Jeri L. Sackett (425) 261-3690.

FEBRUARY 1-4, 2001: 27th Annual Predoctoral Education Conference. Long Beach Hilton, Long Beach, CA. Contact Society of Teachers of Family Medicine (800) 274-2237, ext. 5415; www.STFM.org.

FEBRUARY 11-15, 2001: International Congress XIV on Endovascular Interventions. Arizona Heart Institute Foundation at the Phoenician, Scottsdale, AZ. Contact Erika Scott (602) 604-5030; Fax (602) 604-5020; escott@azheart.com; www.endovascularcongress.org.

FEBRUARY 15-17, 2001: Pri-Med West. Pri-Med at Long Beach Convention Center, Long Beach, CA. 16 hrs Cat 1. Contact Pri-Med (877) 477-4633 (4PRI-MED); www.pri-med.com.

FEBRUARY 18-22, 2001: Pediatric Potpourri State of the Art 2001. University Children's Medical Group, Westin Maui Hotel, Maui, HI. 21.5 hrs Cat 1. Contact Bernadette Serran (323) 669-2305.

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FEBRUARY 28-MARCH 4, 2001: 21st Annual Conference on Families and Health. Kiawah Island Resort, Kiawah Island, SC. Contact Society of Teachers of Family Medicine (800) 274-2237, ext. 5415; www.STFM.org.

MARCH 2001: 3rd Update in Geriatric Psychiatry. University of Colorado School of Medicine, Location to be announced. Cat 1 hrs. Contact Office of Continuing Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065; www.uchsc.edu/cme.

MARCH 3-10, 2001: 29th Annual Diagnostic & Therapeutic Skills in Internal Medicine. University of Southern California Keck School of Medicine, Mauna Kea Resort, Big Island, HI. 27 hrs Cat 1. Contact Ilona Malley (800) USC-1119.

MARCH 4-9, 2001: 21st Annual Mammoth Mountain Emergency Medicine Conference. California Chapter of the American College of Emergency Physicians and Medical Conferences, Inc. in conjunction with the American College of Emergency Physicians, Mammoth Lakes, CA. 18 hrs Cat 1. Contact Dan Abbott, M.D., 504 Evening Star Lane, Newport Beach, CA 92660, (949) 650-4156.

MARCH 8-10, 2001: The Sixth International Conference on Continuous Renal Replacement Therapy. The Hotel del Coronado, Sand Diego, CA. Contact Shirley Kolkey, Complete Conference Management (619) 299-6673; Fax (619) 299-6675; c-c-m@worldnet.att.net.

MARCH 14-16, 2001: Annual Review in Family Medicine: Controversies and Challenges in Primary Care. University of California, San Francisco School of Medicine, Cathedral Hill Hotel, San Francisco, CA. 16 Cat 1 hrs. Contact Program Coordinator (415) 476-5250, Fax (415) 476-6051.

MARCH 24, 2001: 2001 Update in Gastroenterology for the Primary Care Physician. UC Davis Health System, Division of Gastroenterology, Department of Internal Medicine, Office of CME, and Veterans Affairs Northern California Health Care System at UCDMC Cancer Center Auditorium, Sacramento, CA. 3.5 hrs Cat 1. Contact Office of CME (916) 734-5390; Fax (916) 734-8966; web.ucdmc.ucdavis.edu/edu.

MARCH 28-April 3, 2001: AIDS Vaccines in the New Millennium. University of Colorado School of Medicine, Keystone Resort, Keystone, CO. Cat 1 hrs. Contact Office of Continuing Education (800) 882-9153 or (303) 372-9050, Fax (303) 372-9065; www.uchsc.edu/cme.

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Send CME listings for publication to:

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ACADEMIC GENERAL INTERNIST/CLINICIAN-EDUCATOR—The University of California, Davis, Department of Internal Medicine, Division of General Medicine is recruiting one full-time Assistant/Associate Professor level faculty member to serve as a general internist/clinician-educator. Responsibilities will include direct patient care and resident/student teaching of inpatient internal medicine, general medicine consultation, and ambulatory medicine. The candidate will also have significant responsibilities in residency program development and implementation, as well as in medical school curriculum development. The candidate will have a small individual practice in the outpatient clinic. The candidate should have experience in, and a strong commitment to, the education of residents and medical students. Candidates must possess a M.D. degree, be Board certified/eligible in Internal Medicine, and be eligible for licensure in the State of California.

Please forward Curriculum Vitae to Richard White, M.D., c/o Terri McGann, Department of Internal Medicine, Division of General Medicine, University of California, Davis, P.O. Box 179002, Sacramento, CA 95817-9002. This position is open until filled but no later than February 28, 2001. The University of California, Davis is an affirmative action/equal opportunity employer.

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City of Los Angeles Occupational Health Services
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University of California-San Diego–San Diego State University General Preventive Medicine Residency Program The University of California, San Diego (UCSD)–San Diego State University (SDSU) General Preventive Medicine Residency Program is seeking applicants for PGY-2 positions. This two-year program, founded in 1983, prepares physicians for academic, public or private-sector careers in preventive medicine and public health. Areas of emphasis in the program include medically underserved health care, cancer prevention and epidemiology, college health, and population based approaches to sports and exercise medicine. The program includes completion of the MPH degree at SDSU and offers elective experiences at each co-sponsoring institution. Candidates must be eligible for licensure in California including at least a one-year internship. Board eligible/board-certified physicians from other specialties are encouraged to apply. Interested applicants should forward a cover letter with curriculum vitae to Dr. Linda Hill, Program Director, UCSD-SDSU General Preventive Medicine Residency Program, San Diego State University, 5500 Campanile Drive, San Diego, CA 92182-4701, Telephone: (619) 594-5332, Fax: (619) 594-5613, or e-mail pmr@mail.sdsu.edu.

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David Heiden

Baby goats in a thorn branch pen, Somalia, 1982

9445

David Heiden is an ophthalmologist practicing in San Francisco.

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